Urology Services Inquiry

Urology Services Inquiry | 1 Bradford Court | Belfast BT8 6RB
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Mr. Mark Haynes
Consultant Urologist
Southern Health and Social Care Trust
Headquarters
68 Lurgan Road
Portadown
BT63 5QQ

12 October 2023

Dear Sir,

Re: The Statutory Independent Public Inquiry into Urology Services in the Southern Health and Social Care Trust

Provision of a Section 21 Notice requiring the provision of evidence in the form of a written statement

I am writing to you in my capacity as Solicitor to the Independent Public Inquiry into Urology Services in the Southern Health and Social Care Trust (the Urology Services Inquiry) which has been set up under the Inquiries Act 2005 ('the Act').

I enclose a copy of the Urology Services Inquiry's Terms of Reference for your information.

You will be aware that the Inquiry has commenced its investigations into the matters set out in its Terms of Reference. The Inquiry is continuing with the process of gathering all of the relevant documentation from relevant departments, organisations and individuals. In addition, the Inquiry has also now begun the process of requiring individuals who have been, or may have been, involved in the range of matters which come within the Inquiry's Terms of Reference to provide written evidence to the Inquiry panel.

The Urology Services Inquiry is now issuing to you a Statutory Notice (known as a Section 21 Notice) pursuant to its powers to compel the provision of evidence in the form of a written statement in relation to the matters falling within its Terms of Reference.

This Notice is issued to you due to your held posts, within the Southern Health and Social Care Trust, relevant to the Inquiry's Terms of Reference.

The Inquiry is of the view that in your roles you will have an in-depth knowledge of matters that fall within our Terms of Reference. The Inquiry understands that you will have access to all of the relevant information required to provide the witness statement required now, or at any stage throughout the duration of this Inquiry. Should you consider that not to be the case, please advise us of that as soon as possible.

The Schedule to the enclosed Section 21 Notice provides full detail as to the matters which should be covered in the written evidence which is required from you. As the text of the Section 21 Notice explains, you are required by law to comply with it.

Please bear in mind the fact that the witness statement required by the enclosed Notice is likely (in common with many other statements we will request) to be published by the Inquiry in due course. It should therefore ideally be written in a manner which is as accessible as possible in terms of public understanding.

You will note that certain questions raise issues regarding documentation. As you may be aware the Trust has responded to our earlier Section 21 Notice requesting documentation from the Trust as an organisation. However if you in your personal capacity hold any additional documentation which you consider is of relevance to our work and is not within the custody or power of the Trust and has not been provided to us to date, then we would ask that this is also provided with this response.

If it would assist you, I am happy to meet with you and/or your legal representative(s) to discuss what documents you have and whether they are covered by the Section 21 Notice.

You will also find attached to the Section 21 Notice a Guidance Note explaining the nature of a Section 21 Notice and the procedures that the Inquiry has adopted in relation to such a notice. In particular, you are asked to provide your evidence in the form of the template witness statement which is also enclosed with this correspondence. In addition, as referred to above, you will also find enclosed a copy of the Inquiry's Terms of Reference to assist you in understanding the scope of the Inquiry's work and therefore the ambit of the Section 21 Notice.

Given the tight time-frame within which the Inquiry must operate, the Chair of the Inquiry would be grateful if you would comply with the requirements of the Section 21 Notice as soon as possible and, in any event, by the date set out for compliance in the Notice itself.

If there is any difficulty in complying with this time limit you must make an application to the Chair for an extension of time before the expiry of the time limit, and that application must provide full reasons in explanation of any difficulty.

Finally, I would be grateful if you could acknowledge receipt of this correspondence and the enclosed Notice by email to Personal Information redacted by the USI.

Please do not hesitate to contact me to discuss any matter arising.

Yours faithfully

Anne Donnelly
Solicitor to the Urology Services Inquiry

Tel: Personal Information redacted by the USI
Mobile: Personal Information redacted by the USI

Issued by the Urology Services Inquiry on 12/10/2023. Annotated by the Urology Services Inquiry.

THE INDEPENDENT PUBLIC INQUIRY INTO
UROLOGY SERVICES IN THE
SOUTHERN HEALTH AND SOCIAL CARE TRUST

Chair's Notice

[No 20 of 2023]

pursuant to Section 21(2) of the Inquiries Act 2005

WARNING

If, without reasonable excuse, you fail to comply with the requirements of this Notice you will be committing an offence under section 35 of the Inquiries Act 2005 and may be liable on conviction to a term of imprisonment and/or a fine.

Further, if you fail to comply with the requirements of this Notice, the Chair may certify the matter to the High Court of Justice in Northern Ireland under section 36 of the Inquiries Act 2005, where you may be held in contempt of court and may be imprisoned, fined or have your assets seized.

TO: **Mr. Mark Haynes**
Consultant Urologist
Southern Health and Social Care Trust
Headquarters
68 Lurgan Road
Portadown
BT63 5QQ

Issued by the Urology Services Inquiry on 12/10/2023. Annotated by the Urology Services Inquiry.

IMPORTANT INFORMATION FOR THE RECIPIENT

1. This Notice is issued by the Chair of the Independent Public Inquiry into Urology Services in the Southern Health and Social Care Trust on foot of the powers given to her by the Inquiries Act 2005.

2. The Notice requires you to do the acts set out in the body of the Notice.

3. You should read this Notice carefully and consult a solicitor as soon as possible about it.

4. You are entitled to ask the Chair to revoke or vary the Notice in accordance with the terms of section 21(4) of the Inquiries Act 2005.

5. If you disobey the requirements of the Notice it may have very serious consequences for you, including you being fined or imprisoned. For that reason you should treat this Notice with the utmost seriousness.

WITNESS STATEMENT TO BE PRODUCED

TAKE NOTICE that the Chair of the Independent Public Inquiry into Urology Services in the Southern Health and Social Care Trust requires you, pursuant to her powers under section 21(2)(a) of the Inquiries Act 2005 ('the Act'), to produce to the Inquiry a Witness Statement as set out in the Schedule to this Notice by noon **on 2nd November 2023.**

APPLICATION TO VARY OR REVOKE THE NOTICE

AND FURTHER TAKE NOTICE that you are entitled to make a claim to the Chair of the Inquiry, under section 21(4) of the Act, on the grounds that you are unable to comply with the Notice, or that it is not reasonable in all the circumstances to require you to comply with the Notice.

If you wish to make such a claim you should do so in writing to the Chair of the Inquiry at: **Urology Services Inquiry, 1 Bradford Court, Belfast, BT8 6RB** setting out in detail the basis of, and reasons for, your claim by noon **on 26th October 2023**.

Issued by the Urology Services Inquiry on 12/10/2023. Annotated by the Urology Services Inquiry.

Upon receipt of such a claim the Chair will then determine whether the Notice should be revoked or varied, including having regard to her obligations under section 21(5) of the Act, and you will be notified of her determination.

Dated this day 12th October 2023

Signed: 

Christine Smith QC
Chair of Urology Services Inquiry

Urology Services Inquiry

SCHEDULE

[No 20 of 2023]

Monopolar and Bipolar Resection

1. The Policy on the Surgical Management of Endoscopic Tissue Resection HSS(MD)14/2015 was introduced in May 2015 (WIT-54032-54055).

   The policy refers to the 'significantly improved safety profile' for bipolar techniques, noting that *'Significantly, the TUR syndrome has not been reported with bipolar equipment. A recent systematic review and meta-analysis comparing traditional monopolar TURP with bipolar TURP established in 22 trials that the TUR syndrome was reported in 35/1375 patients undergoing M-TURP and in none of the 1401 patients undergoing B-TURP. Even taking into account that one study alone was responsible for 17 of the 35 cases, the accompanying editorial states, "the elimination of TUR syndrome alone has been a worthy consequence of adopting bipolar technology.'"* [WIT-54041]

   At [WIT54042], it is noted that: *'NICE, in February 2015, also issued guidance for the public on this topic. They indicated that, "the TURis system can be used instead of a surgical system called 'monopolar transurethral resection of the prostate'. Healthcare teams may want to use the TURis system instead of monopolar TURP because there is no risk of a rare complication called transurethral resection syndrome and it is less likely that a blood transfusion after surgery will be needed. Therefore, the case for moving from a monopolar to bipolar technique for resection of the prostate would appear to be well established as safer with regard to the development of the TUR syndrome…'*

   In your statement to the Inquiry (at WIT-53948-53949), you state as follows:

   '*In August 2015, HSS(MD)14/2015 required trusts to take action with regard to a regional policy on the surgical management of endoscopic tissue resection. For urology teams this related to switching from monopolar transurethral*

resection (in glycine) to bipolar resection (in saline), with the work on the policy having been commissioned following a coroners verdict in October 2015. Mr O'Brien engaged in the process of assessment of new bipolar resection equipment. However, he subsequently expressed the view that he would be continuing to use monopolar resection in glycine, thereby not conforming with the policy. On reflection, this unwillingness to conform with recommendations from others should have provoked concern regarding wider aspects of his practice, especially with regards to delivering treatment in line with NICE guidance/MDM.'

Having regard to the above, and to the oral and written evidence of Mr Chris Hagan, concerning the introduction of bipolar resection located at TRA-07909 to TRA-07914 and WIT-98866 to WIT-98867, you are now asked to address the following:

(a) Please provide a narrative account of your experience initially with the use of monopolar resection instruments within the Southern Trust.

(b) Did you believe the use of monopolar with glycine irrigation was a safe method of performing TURP procedures?

(c) When did you become aware of a regional approach, led by Dr Julian Johnston, to develop a policy on the use of irrigating fluids and the Coroner's decision which prompted it? (WIT-99100-WIT-99101)? Please confirm when, and how, you first became aware of (i) the intention to switch from monopolar resection to bipolar resection and (ii) the policy referred to above.

(d) Please provide full details of any involvement you had in the 'process of assessment of new bipolar resection equipment' to include details of:

i. The nature and purpose of this assessment;
ii. When the assessment took place and the duration of same;
iii. The identities of others involved in assessing the equipment;
iv. Any conclusions reached as a result of this assessment.

(e) When did the Southern Trust direct the cessation of monopolar procedures?

(f) Did you continue to undertake monopolar resection in glycine beyond this point? If yes, please answer the following:

i. Were others aware that you continued to do so? If so, please identify those individuals and explain how they were so aware.

ii. Did others continue to undertake these procedures at this time?

iii. Mr O'Brien indicated via email in March 2016 that he would 'not use or try bipolar resection again' (TRU-395978). Do you consider the explanation he offers therein to be valid?

iv. When did you cease undertaking these procedures, and why?

(g) What was your view on the introduction of bipolar resection with saline? Did you believe it to be a suitable alternative? Why/ why not?

(h) The Trust purchased this equipment in January 2018 (TRU-395981). Were you concerned by the significant delay in the purchase and introduction of this equipment?

(i) Was training required to adapt to the new equipment and technique? If yes, please provide details of all such training you received.

2. In his statement to the Inquiry (at WIT-98867), Mr Chris Hagan states as follows:

'Some years after the policy was developed I was contacted by phone by Dr Charlie McAllister, a consultant anaesthetist in CAH. I cannot be sure when exactly I received this call, but I believe it was sometime between 2017 and 2019. Dr McAllister wished to discuss TUR surgery, TUR syndrome and use of bipolar resection. He explained that they had an issue in CAH with an individual surgeon carrying out prolonged TURP resections with glycine and some "bad" TUR syndromes. He did not name the surgeon specifically. He wanted to know

my experience with introducing TURP in saline. I explained that the experience in Belfast was good, that the technique was similar to monopolar TURP with glycine and that with modern equipment, in my view, it was unjustified and unsafe to continue to use glycine due to the safety profile of it as an irrigating fluid. From a personal perspective, I have carried out TURP in saline for around 10 years and see no justification for the use of glycine.'

(a) Were you aware that Dr McAllister contacted Mr Hagan concerning this issue?

(b) Had this issue been brought to your attention as AMD for Surgery and Elective Care (Oct 17 – Aug 21) or as Clinical Director for Surgery (June 16 – Sept 17), prior to Dr McAllister's communication? If so, please provide full details of all discussions relating to this issue, to include dates, the identities of parties to the discussions, the content of those discussions and any actions taken by you, or others, on foot of same.

3. In oral evidence to the Inquiry on Day 61 (19th September 2023, Mr Hagan described the introduction of bipolar technique within the Belfast Trust ('BHSCT') as follows:

'We introduced bipolar in Belfast in 2013, we took all the monopolar sets out and the whole team moved over to bipolar without any real issue.' [TRA-07913]

'I didn't find it difficult introducing it in Belfast, because all the team that I work with focus on patient safety and they put patient safety before their own personal preferences. And the data was compelling on this. And I think it's really important to use data to inform your decisions. And if you have a technique that's demonstrably safer, I don't understand why you wouldn't adopt it.' [TRA-07914]

(a) To the extent that you are able to assist the Inquiry, please explain the reason(s) for the apparent delay in introducing the bipolar approach within the Southern Trust, as compared with BHSCT.

(b) Were you concerned by any delay in the introduction of this approach?

NOTE:

By virtue of section 43(1) of the Inquiries Act 2005, "document" in this context has a very wide interpretation and includes information recorded in any form. This will include, for instance, correspondence, handwritten or typed notes, diary entries and minutes and memoranda. It will also include electronic documents such as emails, text communications and recordings. In turn, this will also include relevant email and text communications sent to or from personal email accounts or telephone numbers, as well as those sent from official or business accounts or numbers. By virtue of section 21(6) of the Inquiries Act 2005, a thing is under a person's control if it is in his possession or if he has a right to possession of it.

Urology Services Inquiry

UROLOGY SERVICES INQUIRY

USI Ref: Section 21 Notice Number 20 of 2023
Date of Notice: 12th October 2023

Monopolar and Bipolar Resection

1. The Policy on the Surgical Management of Endoscopic Tissue Resection HSS(MD)14/2015 was introduced in May 2015 (WIT-54032-54055).

   The policy refers to the 'significantly improved safety profile' for bipolar techniques, noting that *'Significantly, the TUR syndrome has not been reported with bipolar equipment. A recent systematic review and meta-analysis comparing traditional monopolar TURP with bipolar TURP established in 22 trials that the TUR syndrome was reported in 35/1375 patients undergoing M-TURP and in none of the 1401 patients undergoing B-TURP. Even taking into account that one study alone was responsible for 17 of the 35 cases, the accompanying editorial states, "the elimination of TUR syndrome alone has been a worthy consequence of adopting bipolar technology.'"* [WIT-54041]

   At [WIT54042], it is noted that: *'NICE, in February 2015, also issued guidance for the public on this topic. They indicated that, "the TURis system can be used instead of a surgical system called 'monopolar transurethral resection of the prostate'. Healthcare teams may want to use the TURis system instead of monopolar TURP because there is no risk of a rare complication called transurethral resection syndrome and it is less likely that a blood transfusion after surgery will be needed. Therefore, the case for moving from a monopolar to bipolar technique for resection of the prostate would appear to be well established as safer with regard to the development of the TUR syndrome…'*

   In your statement to the Inquiry (at WIT-53948-53949), you state as follows:

'*In August 2015, HSS(MD)14/2015 required trusts to take action with regard to a regional policy on the surgical management of endoscopic tissue resection. For urology teams this related to switching from monopolar transurethral resection (in glycine) to bipolar resection (in saline), with the work on the policy having been commissioned following a coroners verdict in October 2015. Mr O'Brien engaged in the process of assessment of new bipolar resection equipment. However, he subsequently expressed the view that he would be continuing to use monopolar resection in glycine, thereby not conforming with the policy. On reflection, this unwillingness to conform with recommendations from others should have provoked concern regarding wider aspects of his practice, especially with regards to delivering treatment in line with NICE guidance/MDM.'*

Having regard to the above, and to the oral and written evidence of Mr Chris Hagan, concerning the introduction of bipolar resection located at TRA-07909 to TRA-07914 and WIT-98866 to WIT-98867, you are now asked to address the following:

(a) Please provide a narrative account of your experience initially with the use of monopolar resection instruments within the Southern Trust.

1.01 Monopolar resection was a standard mode of transurethral resection throughout my training and initial years as a Consultant, while bipolar resection equipment had been available for many years it was not used as standard across Urology units. At the time of my move to Southern Trust in 2014, I had been using monopolar resection in my previous consultant job and therefore it was of no concern to me that monopolar resection was the equipment used in the Southern Trust. The monopolar resection sets available in the Southern Trust were the same as those I had used in my previous employment.

1.02 At the time that I commenced employment in the Southern Trust I do not recall being made aware of the Coroner's ruling and I am subsequently aware it was circulated in 2013. It is my recollection that there was a single bipolar resection set available for use at this time. Surgeons were able to choose to use this for suitable cases. However, it is my recollection that this particular bipolar resection kit was not as effective as the newer equipment available on the

market at this time.

1.03 TUR syndrome as a complication of monopolar resection in glycine is a well recognised risk in urology trans-urethral surgery. As trainees we learnt how to identify and manage the condition and it was a regular topic within FRCS (Urol). Like all urologists, I have managed patients with TUR syndrome as a consequence of glycine absorption during transurethral resection. Awareness of the risk of this complication and monitoring / communication during surgery has always been a fundamental aspect of ensuring patient safety during transurethral resection (and indeed all surgery). An incident report regarding a patient I operated on in 2015 (*see 1. incident ID* Irrelevant redacted by the USI who developed transurethral syndrome identifies this team awareness and the importance of good team communication, as demonstrated in the case, in the early identification of a patient at risk of this complication and its management.

1.04 In the Southern Trust the standard procedures which I undertook which utilised glycine were TURP and TURBT. Recognising the risks of TUR syndrome, as standard practice while operating I was always conscious of the resection time and endeavoured to keep this to a minimum and in particular would look to avoid resecting for longer than sixty minutes where possible. With regards resection time, the GIRFT document 'Towards better care for patients with bladder outflow obstruction' states '*Traditionally, TURP has been associated with an operative time of 60-90 minutes…*', (*see 2. GIRFT Report*) and the EAU 'Management of non-neurogenic Male LUTS' guidelines note with regards Monopolar TURP *'… the procedure is safest when performed in under 90 minutes.' (see 3. EAU-Guidelines-on-Non-Neurogenic-Male-LUTS-2023)*. Despite the standard measures TUR syndromes did occur, typically with TURP procedures as the risk of glycine absorption is much higher in this procedure than TURBT. I have no recollection of experiencing a TUR syndrome in a TURBT procedure. As the surgical and anaesthetic teams are very well aware of the risks of TUR syndrome these were identified and managed appropriately.

1.05 Notwithstanding my comments regarding the inferiority of the bipolar resection set available in the Southern trust prior to January 2018, I did use this on occasion, in particular in patients with whom monopolar diathermy carried additional concerns for example with patients with pacemakers. Due to the

nature of my practice which is predominantly urology oncology, compared with my peers, I performed relatively small numbers of TURPs.

(b) Did you believe the use of monopolar with glycine irrigation was a safe method of performing TURP procedures?

1.06 As detailed above monopolar TUR with glycine irrigation carries a risk of TUR syndrome which the surgical, anaesthetic and nursing teams within Southern Trust were aware of and identified and managed appropriately (as illustrated in *1. Incident ID* [Irrelevant redacted by the USI]. Bipolar resection systems were available which reduced the risk of TUR syndrome although the risk of fluid (saline) absorption remain, but this presents a lower risk to patients. At the time, it is my understanding, monopolar resection was a standard method utilised in many Urology units throughout the NHS. It remains the case that monopolar transurethral resection (in glycine) and bipolar transurethral resection (in saline) are amongst the NICE approved surgical treatments for male bladder outflow obstruction (*see 4. NICE CG97*) and are amongst the standard surgical treatment options identified in the 2022 GIRFT report *'Urology: towards better care for patients with bladder outlet obstruction'* publication (updated August 2023). The European association of Urology Guidelines '*Management of Non-neurogenic male LUTS (2023)*' recommendations regarding transurethral resection surgery state '*Offer bipolar- or monopolar-transurethral resection of the prostate to surgically treat moderate-to-severe LUTS in men with prostate size of 30-80 mL.'*

1.07 Bipolar resection in saline offers an alternative to monopolar resection in glycine and does not carry a risk of 'TUR syndrome' and therefore from this perspective is safer. However, appropriate equipment needs to be available, and this was not the case in Southern Trust until after the equipment was purchased in January 2018. An action plan was introduced by the Trust to mitigate risk on 23rd November 2015, by ensuring that fluid absorption was identified early, and regular monitoring took place of sodium levels, in order to detect falls in serum sodium before patients became symptomatic. This ensured that monopolar resection in glycine could be delivered safely, in the absence of appropriate bipolar equipment (*see 5.-9. 20151123 Final Draft Action Plan re Surgical Management of Endo Tissue Resection, A1-A4*).

(c) When did you become aware of a regional approach, led by Dr Julian Johnston, to develop a policy on the use of irrigating fluids and the Coroner's decision which prompted it? (WIT-99100-WIT-99101)? Please confirm when, and how, you first became aware of (i) the intention to switch from monopolar resection to bipolar resection and (ii) the policy referred to above.

1.08 I became aware of the regional approach in December 2014 when it was circulated. At the time, having read the summary presentation to DHSSPS/Medical Leaders Forum which had taken place on 3 November 2014 by Julian Johnston, I replied by email with some early thoughts on this *(see 10. 20141231 - E M Haynes Medical Leaders Forum).* In my reply I made note that the presentation had referred to evidence being sought from a variety of organisations which did not include either the Royal College of Surgeons or the British Association of Urological Surgeons which I was surprised at, given trans-urethral resection in glycine had been standard urological practice over many decades. I also commented that the direction of travel was clearly towards bipolar resection and it was my view this was not something we would be able to resist. I highlighted that to switch to bipolar resection would require investment. I also highlighted that a fluid management system which had been purchased by the Trust was not suitable for transurethral resection. This was because it produced a pulsed flow rather than continuous flow which led to vision issues particularly when bleeding was encountered during surgery. As a result of the issue with this fluid management system, I stated it was not fit for purpose and would not be used for transurethral surgery unless modifications were made to render it fit for purpose.

1.09 Only the minutes of the Medical Leaders meeting were circulated at this time. I have no recollection of the first draft of the policy being circulated to us at this time or copies of the presentation (as is stated in the action point from this meeting). The first email including a draft policy that I have been able to locate received by me is from March 2015 (*see 11.-12.20150304 E re Policy on Surgery for Endoscopic Tissue Resection V3,A1).* The final policy I first received on 9th September 2015 (*see 13.-14. 20150909 Policy on the Surgical Management of Endo Tissue Resection, A1)* and as referred to at paragraph 1.07, an action plan

within the Trust was developed and circulated on 23rd November 2015 (*see 5.-9. 20151123 Final Draft Action Plan re Surgical Management of Endo Tissue Resection, A1-A4*).

(d) Please provide full details of any involvement you had in the 'process of assessment of new bipolar resection equipment' to include details of:

i. The nature and purpose of this assessment;

1.10 The nature of the assessment was a trial of available bipolar equipment for Urological procedures wherein the Urologists assessed the equipment during procedures providing a rating against a number of factors, with the purpose of identifying the most suitable/cost-effective system to recommend for purchase in order to switch to bipolar resection.

ii. When the assessment took place and the duration of same;

1.11 I cannot recall definitively when the assessment commenced nor the duration. However, it is noted as being undertaken in the draft action plan circulated on 23rd November 2015 (*see 5.-9. 20151123 Final Draft Action Plan re Surgical Management of Endo Tissue Resection, A1-A4*) and the review outcome was discussed at the Departmental Meeting on 22 September 2016 (I was not present at the meeting as I was Urologist of the Week and was unavailable due to this clinical commitment). However, in the minutes of this meeting comment is made that the outcome had been discussed with me later that day and I had no concern with the agreed view (noted as unanimous in the minutes) of my colleagues to recommend the purchase of the STORZ system (*see 15.-17. 20161012 Urology Department Minutes 22 9 2016, A1-A2*). The Trial evaluation criteria and equipment specification are as detailed in the 'Saline resection Trial review and evaluation sept '16' document circulated with these minutes.

iii. The identities of others involved in assessing the equipment;

1.12 The Urology Consultants at the time, namely myself, Mr Young, Mr

O'Brien, Mr Glackin, Mr O'Donoghue and Mr Suresh. The Specialty Registrars and Specialty Doctor in post at this time were also involved, namely Mr Matthew Tyson, Mr Bashir Mukhtar and Ms Jenny Martin. The Theatre Nurses in post at the time and involved in the assessment were Sr Susan England and Sr Pamela Johnston.

iv. Any conclusions reached as a result of this assessment.

1.13 The conclusion reached from this trial are summarised in the urology departmental meeting minutes from 22/09/23, *(see 15.-17. 20161012 Urology Department Minutes 22 9 2016, A1-A2)* namely that the STORZ bipolar resection system was to be the preferred system for purchase for the urology service.

(e) When did the Southern Trust direct the cessation of monopolar procedures?

1.14 It is my understanding that the regional policy did not direct that all monopolar procedures should stop, rather that trusts ***'Introduce Bipolar equipment using saline, regionally; curtail the use of glycine as a irrigant, strictly monitor when it is still used and eventually stop when there ceases to be circumstances when glycine use is considered the safest'.***

1.15 The Trust endorsed the policy in November 2015 and an action plan to implement the policy was circulated. Mr Young, as Clinical lead for urology states in an email sent on 16th November 2017 *(see 18. 20171117 E re Saline TURP issue)* '*…a defined date to transfer over to the new system was needed. We defined this date as 1st January 2018. This date was defined as fitting a timeline that allowed for the trail period, quotes to be received, assessment and providing the Trust a reasonable period of time to purchase the equipment*…'. As detailed at paragraph 1.07 above, the bipolar resection equipment was not purchased until January 2018 and therefore the Urologists in Southern Trust were not in a position to switch to bipolar resection until after January 2018. From recollection it remained the case that in certain instances, such as when a long resectoscope was required, the only available equipment remained a

monopolar set which necessitated resection in glycine. Also, where a 'whip' electrode is used for cystodiathermy (cauterizing small abnormalities in the bladder or cauterizing after 'cold-cup biopsy' using a narrower cystoscope rather than a resectoscope) this is also a monopolar instrument which utilized either water of glycine as the irrigant.

(f) Did you continue to undertake monopolar resection in glycine beyond this point? If yes, please answer the following:

1.16 After the bipolar resection equipment had been purchased I switched to using this (and therefore undertaking transurethral resection in saline and not glycine). I understand that monopolar equipment and glycine remain available for instances where bipolar resection is not appropriate (eg the long resectoscope only had monopolar kit available, or to use the 'whip' electrode for cystodiathermy – this is a monopolar piece of equipment), with monitoring in place as described in the policy and action plan.

i. Were others aware that you continued to do so? If so, please identify those individuals and explain how they were so aware.

1.17 I do not have any specific recollection of electing to use monopolar resection after the bipolar equipment had been purchased. However, as noted there may have been rare instances where the only available equipment was monopolar. The resection medium / technology is identified at the team brief for each case and so if glycine was used it was identified and the monitoring arrangements as described in the policy / action plan put in place.

ii. Did others continue to undertake these procedures at this time?

1.18 Transurethral resection is a surgical procedure performed by all urologists in both elective and emergency settings. Having purchased the equipment in January 2018, and the entire urology team in Southern Trust having been involved in the decision-making process, I was of the impression that the whole team had switched to bipolar resection. It is my understanding that this was the case for all my consultant colleagues in Southern Trust, who also switched to bipolar transurethral resection as their standard technology for transurethral

resection, with the exception of Mr O'Brien. However, I was not aware of this at the time. Mr O'Brien was present at the urology departmental meeting on 22/9/16 where the view is noted as 'unanimous' that the STORZ bipolar resection equipment was recommended for purchase. It is also noted in Mr Young's email dated 16th November 2017 (*see 18. 20171117 E re Saline TURP issue*) that *'…Urologists in the department will be maintaining their position for a switch to using saline to perform TURP as of 1st January 2018'*. Consultants do not attend each other's operating lists and therefore I did not have an opportunity to identify that he was continuing to use monopolar resection. I do not have any specific recollection of being made aware by others that Mr O'Brien continued to use monopolar resection in glycine.

iii. Mr O'Brien indicated via email in March 2016 that he would 'not use or try bipolar resection again' (TRU-395978). Do you consider the explanation he offers therein to be valid?

1.19 I do not consider the explanation offered to be valid. Surgical technology changes / evolution can impact on procedures in different ways. For some equipment (e.g., for robotic surgery) full formal training to undertake the 'new' procedure using the new equipment is required. For other changes / innovations, the new equipment is used in place of a previous item (e.g., ultrasonic 'scalpel' in place of scissor or steel blade). The surgical technique is unchanged, and the surgeon needs to learn how to use the technology safely and effectively. This training support is typically provided by representatives from the company supplying the equipment. Comment on the support provided by the supplier formed part of the appraisal of the bipolar systems undertaken in Southern Trust and is commented on in the report for each supplier.

1.20 With regards bipolar resection, the equipment is used in the same way as monopolar equipment, with the exception being that in order to improve coagulation during 'cut' the resection loop needs to be moved through the tissue being resected more slowly. Contrary to the views expressed by Mr O'Brien and as stated in the GIRFT 'Urology – towards better care for patients with bladder outflow obstruction' bipolar transurethral resection systems along with other newer techniques for performing bladder outflow surgery *'…have been adopted to reduce blood loss and length of stay…'*. While other newer

surgical techniques require training in delivering a new procedure (e.g., laser techniques), an advantage of bipolar transurethral resection is that the equipment and surgical technique is the same as that of monopolar resection and so a switch from monopolar to bipolar equipment does not require significant retraining, merely a minor adaption of surgical technique and a familiarity with the new equipment.

1.21 It should be expected that surgeons feel some apprehension / concern when switching from a standard piece of equipment that they have used effectively for many years. The email views (attachments below) from May 2015 from urologists across the region demonstrate broad support across NI for the switch to bipolar systems, with some concern expressed being in relation to TURBT and in particular, a concern regarding impact on pathological interpretation of the specimen. Views expressed by colleagues in Belfast Trust, who had switched to bipolar resection before the other Trusts were that bipolar was the equipment they used as choice for all transurethral resection.

1.22 As stated in my previous statement, my reflection on the views expressed by Mr O'Brien, and my subsequent awareness that he had continued to utilise glycine transurethral resection are that this should have raised concern in more general terms about Mr O'Brien's approach to external recommendations / guidance that required a change in his practice.

See attachments:

19. 20150528 E from JMcK re Endoscopic Distending Fluids for the Coroner
20. 20150528 E from JMcK re Endoscopic Distending Fluids for the Coroner A1
21. 20150528 E from JMcK re Endoscopic Distending Fluids for the Coroner A2
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24. 20150528 E from JMcK re Endoscopic Distending Fluids for the Coroner 3
25. 20150528 E from JMcK re Endoscopic Distending Fluids for the Coroner 4

26. 20150528 E from JMcK re Endoscopic Distending Fluids for the Coroner 5

27. 20150528 E from JMcK re Endoscopic Distending Fluids for the Coroner 6

28. 20150528 E from JMcK re Endoscopic Distending Fluids for the Coroner 7

29. 20150528 E from JMcK re Endoscopic Distending Fluids for the Coroner 8

30. 20150528 E from JMcK re Endoscopic Distending Fluids for the Coroner 9

iv. When did you cease undertaking these procedures, and why?

1.23 As per my previous comments at paragraphs 1.16-1.18, once the bipolar resection equipment was in place in Southern Trust from January 2018, I moved to Bipolar resection for all transurethral procedures, with the exception of the rare case as noted previously, where the only available equipment was monopolar.

(g) What was your view on the introduction of bipolar resection with saline? Did you believe it to be a suitable alternative? Why/ why not?

1.24 I had experienced bipolar resection at various points of my urological training. The modern systems developed over time now offer an equivalence to monopolar surgery. While professional guidelines continue to support the use of either bipolar or monopolar systems, it is recognized that resection in saline and therefore bipolar resection, eliminates the risk of TUR syndrome and therefore has a favourable safety profile. Therefore, providing appropriate equipment is available, I supported the switch to bipolar equipment for transurethral resection. My experience of the systems trialled was that the STORZ and Olympus systems were similar and provided a suitable alternative to monopolar transurethral resection.

(h) The Trust purchased this equipment in January 2018 (TRU-395981). Were you concerned by the significant delay in the purchase and introduction of this equipment?

1.25 It was my understanding following the Departmental meeting in September 2016 (referred to at paragraph 1.11) that the STORZ bipolar equipment should be purchased and that the Trust would be moving to provide this equipment to enable us to move to bipolar transurethral resection as soon

as possible. In March 2017 I became aware that this was not the case, with the equipment sitting on a capital list of investments that required funding within the Trust along with a large number of other items required. On the same day, 7th March 2017 I explored the position with regards funding for this kit with the Assistant Director for the Service, Mr Ronan Carroll, by email (*see 42. 20170307 E re Bipolar Resection Kits Funding from MY).* I highlighted we required the equipment to comply with the review recommendations, and suggested we needed to identify our non-compliance with the recommendations of the review on the Trust Risk Register as we (urologists and the Trust) would be open to criticism if we have a significant TUR syndrome while we continue to offer only monopolar resection in Glycine. Unfortunately, it is my understanding that at this time the required funds to purchase this kit were not identified and therefore the equipment was not purchased.

1.26 On 10 September 2017 I was copied in an email requesting a review of medical equipment priority list prior to consideration of funding through the Capital Allocation Group (CAG) (*see 32. 20170915 E re Medical Equipment Capital Priorities*). At this time, I was CD for General Surgery and T&O, however as a Consultant Urologist raised concerns that this equipment was on this list seemingly as an optional purchase for the Trust and raised the vulnerability of our clinical teams in continuing monopolar resection without bipolar options in the presence of a clear regional policy. In the email on 25th October 2017, the impression given was that funding for the purchase of this equipment was approved (*see 33.-34. 20171025 Capital Equipment List for Priority A1*). However, as noted on 16th November 2017 in the email from Mr Young (*see 18. 20171117 E re Saline TURP issue),* this was not the case. Mr Young highlighted that the Urologists would cease the current type of TURP surgery from the 1st January 2018 if the new equipment was not available. I have no definitive recollection of this decision being reached by my colleagues but suspect we would have discussed this amongst the consultants after the Patient Safety Meeting on 15th November 2017 (*see 20171115_Urology MM Minutes)*, as the minutes do not reflect this being discussed. In my email on 17th November 2017, I highlight my understanding that with regards to Theatre equipment, three items had been identified as an equal ‘priority one’ and it appeared that the bipolar equipment had been prioritized as ‘priority two’ by someone else. No funding had been identified at this point for the purchase of

this equipment. I escalated my concerns to the Director of Acute Services in my email of 19 November 2017 (*see 36.-40. 37. 20171119 E re Capital Funding Saline TUR, A1-A4*). In this email I highlighted my concerns regarding the impact of this decision and noted the Clinical Lead for Urology's concerns, as expressed in his email dated 16 November 2017. In addition, I have commented that I would raise this with the Medical Director, however I have no written record of this and anticipate I would have done this verbally. It is my understanding that subsequently the purchase of this required equipment was approved, and this led to the purchase of the equipment in January 2018.

See attachments:

41. 20170307 E Demo Bipolar Sets Funding
42. 20170307 E re Bipolar Resection Kits Funding from MY
32. 20170915 E re Medical Equipment Capital Priorities
33.-34. 20171025 Capital Equipment List for Priority,A1
43. 20171117 E re Update from CAG re Equipment Request
18. 20171117 E re Saline TURP issue
35. 20171115_Urology MM Minutes
36.-40. 20171119 E re Capital Funding Saline TUR, A1, A2, A3, A4

(i) Was training required to adapt to the new equipment and technique? If yes, please provide details of all such training you received.

1.27 I refer to my response to (f) (iii) (paragraphs 1.19-1.22).

2. In his statement to the Inquiry (at WIT-98867), Mr Chris Hagan states as follows:

'Some years after the policy was developed I was contacted by phone by Dr Charlie McAllister, a consultant anaesthetist in CAH. I cannot be sure when exactly I received this call, but I believe it was sometime between 2017 and 2019. Dr McAllister wished to discuss TUR surgery, TUR syndrome and use of

bipolar resection. He explained that they had an issue in CAH with an individual surgeon carrying out prolonged TURP resections with glycine and some "bad" TUR syndromes. He did not name the surgeon specifically. He wanted to know my experience with introducing TURP in saline. I explained that the experience in Belfast was good, that the technique was similar to monopolar TURP with glycine and that with modern equipment, in my view, it was unjustified and unsafe to continue to use glycine due to the safety profile of it as an irrigating fluid. From a personal perspective, I have carried out TURP in saline for around 10 years and see no justification for the use of glycine.'

(a) Were you aware that Dr McAllister contacted Mr Hagan concerning this issue?

2.01 No, I was not aware.

(b) Had this issue been brought to your attention as AMD for Surgery and Elective Care (Oct 17 – Aug 21) or as Clinical Director for Surgery (June 16 – Sept 17), prior to Dr McAllister's communication? If so, please provide full details of all discussions relating to this issue, to include dates, the identities of parties to the discussions, the content of those discussions and any actions taken by you, or others, on foot of same.

2.02 I have no recollection of anyone raising concerns with me regarding '*an individual surgeon carrying out prolonged TURP resections with glycine and some "bad" TUR syndromes',* either during my time as Clinical Director for Surgery (although my responsibilities in this medical management role did not cover Urology), or as Associate Medical Director for Surgery and Elective care.

2.03 During my time working in the Southern Trust from May 2014, I am aware of 1 'TUR syndrome' case that was reported via the incident reporting system (*see 1.Incident ID* Personal information redacted by USI. This was a case that I undertook on 30th March 2015 and the report notes that the surgical time was 55-60 minutes therefore, this was not a prolonged resection.

2.04 I have also had a review of Patient Safety Meeting minutes (previously 'Audit Meetings' and 'Morbidity and Mortality meetings') carried out for the

purposes of answering this question and confirm that during my tenure in the Southern Trust there has been no discussion of cases of TUR syndromes at these meetings.

3. In oral evidence to the Inquiry on Day 61 (19th September 2023, Mr Hagan described the introduction of bipolar technique within the Belfast Trust ('BHSCT') as follows:

'We introduced bipolar in Belfast in 2013, we took all the monopolar sets out and the whole team moved over to bipolar without any real issue.' [TRA-07913]

'I didn't find it difficult introducing it in Belfast, because all the team that I work with focus on patient safety and they put patient safety before their own personal preferences. And the data was compelling on this. And I think it's really important to use data to inform your decisions. And if you have a technique that's demonstrably safer, I don't understand why you wouldn't adopt it.' [TRA-07914]

(a) To the extent that you are able to assist the Inquiry, please explain the reason(s) for the apparent delay in introducing the bipolar approach within the Southern Trust, as compared with BHSCT.

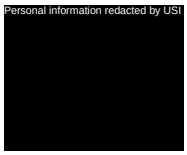
3.01 I understand that the Belfast Trust switched to Saline (bipolar) resection in 2013, before I worked in NI. I was unaware of this at the time I commenced employment in Southern Trust. In Southern Trust the process of trialling the equipment completed in September 2016. The equipment was not subsequently purchased until January 2018. Of note, the decision in November 2017 had been initially made not to assign capital monies to this equipment purchase and it was only the subsequent intervention from the urology team) and myself (*18. 20171117 E re Saline TURP issue*) which led to a change in this decision. It is my understanding that a lack of available funding and competing priorities were the underlying reason behind this delay with decisions made by the Capital Allocation Group (CAG).

(b) Were you concerned by any delay in the introduction of this approach?

3.02 Yes, I was concerned at the delay. I have described my concerns in my emails referenced above at 1 (h) (paragraphs 1.25-1.26).

NOTE:

By virtue of section 43(1) of the Inquiries Act 2005, "document" in this context has a very wide interpretation and includes information recorded in any form. This will include, for instance, correspondence, handwritten or typed notes, diary entries and minutes and memoranda. It will also include electronic documents such as emails, text communications and recordings. In turn, this will also include relevant email and text communications sent to or from personal email accounts or telephone numbers, as well as those sent from official or business accounts or numbers. By virtue of section 21(6) of the Inquiries Act 2005, a thing is under a person's control if it is in his possession or if he has a right to possession of it.

Signed: 

Date: 02/11/2023

Section 21 Notice Number 20 of 2023 – Mark Haynes

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40. 20171119 E re Capital Funding Saline TUR A4
41. 20170307 E Demo Bipolar Sets Funding
42. 20170307 E re Bipolar Resection Kits Funding from MY
43. 20171117 E re Update from CAG re Equipment Request

TUR syndrome Incident

ID	Incident date	Time	Site	Division	Service Area	Speciality	Loc (Exact)	Severity	Description	Action taken	Lessons learned	Approval status	Closed	Directorate	Staff groups
Irrelevan	20/03/2015	16:45	Craigavon Area Hospital	Surgery and Elective Care	ATICS	ANAES	Theatres 1-4 CAH	Minor	A patient developed acute severe hyponatraemia during TURP surgery. He had general anaesthesia with an LMA and spontaneous ventilation (he was very anxious about having a spinal) and had an arterial line inserted after induction. His initial sodium on the ABG was 140 mmol/l. The surgeon told me that the blood loss was more than average and I did an ABG. This was about 30 minutes after surgery commenced. The patient's sodium was 131 mmol/l. I informed the surgeon who decided to limit surgery to the left side. I stopped his IV fluid (450ml of Hartmanns had been given). Fifteen minutes later his sodium was 122mmol/l and surgery was completed as soon as possible. I gave 40mg furosemide IV. Overall surgical time was 55-60 minutes. The patient had 25450 ml of glycine infused and there was 26400ml in the suction. The patient emerged from anaesthesia uneventfully and was transferred to recovery at approximately 17:15. His initial sodium in recovery was 126mmol/l (on an ABG). This was taken within 5 minutes of entering recovery. The patient was asymptomatic and remained so. I discussed him with the ICU consultant on call, who accepted care for the patient in recovery for electrolyte management and the patient was commenced on 1.8% NaCl at 50 ml/h. The lab U&E that was sent at 17:30, reported a sodium of 130mmol/l. He remained in recovery for 24h and was transferred back to the ward on Saturday evening when his sodium was 136mmol/l.	The hyponatraemia was promptly recognised and managed. Care of the patient was kindly taken over by ICU post operatively and the patient's sodium normalised without any adverse effects. The patient was informed that he was remaining in recovery as his sodium levels had fallen and we needed to monitor this closely until it had resolved	All procedures in place worked accordingly. Case discussed at Anaesthetic directorate meeting 17/04/2015. No issue on management. This case illustrates the situation where the fluid deficit can be inexistent and falsly reassuring when actually significant amount of Glycine can be absorbed. This is the case when the surgery is difficult and there is some recorded blood loss. Plan is to reinforce the importance of good communication between all actors in theatre (as done in this case) and close monitor of both sodium and Haemoglobin, especially if unexpected blood loss.	Finally approved	30/03/2015	ACUTE	

Received from Mark Haynes on 03/11/2023. Annotated by the Urology Services Inquiry.

NHS England

GIRFT GETTING IT RIGHT FIRST TIME

The British Association of Urological Surgeons

British Association of Day Surgery

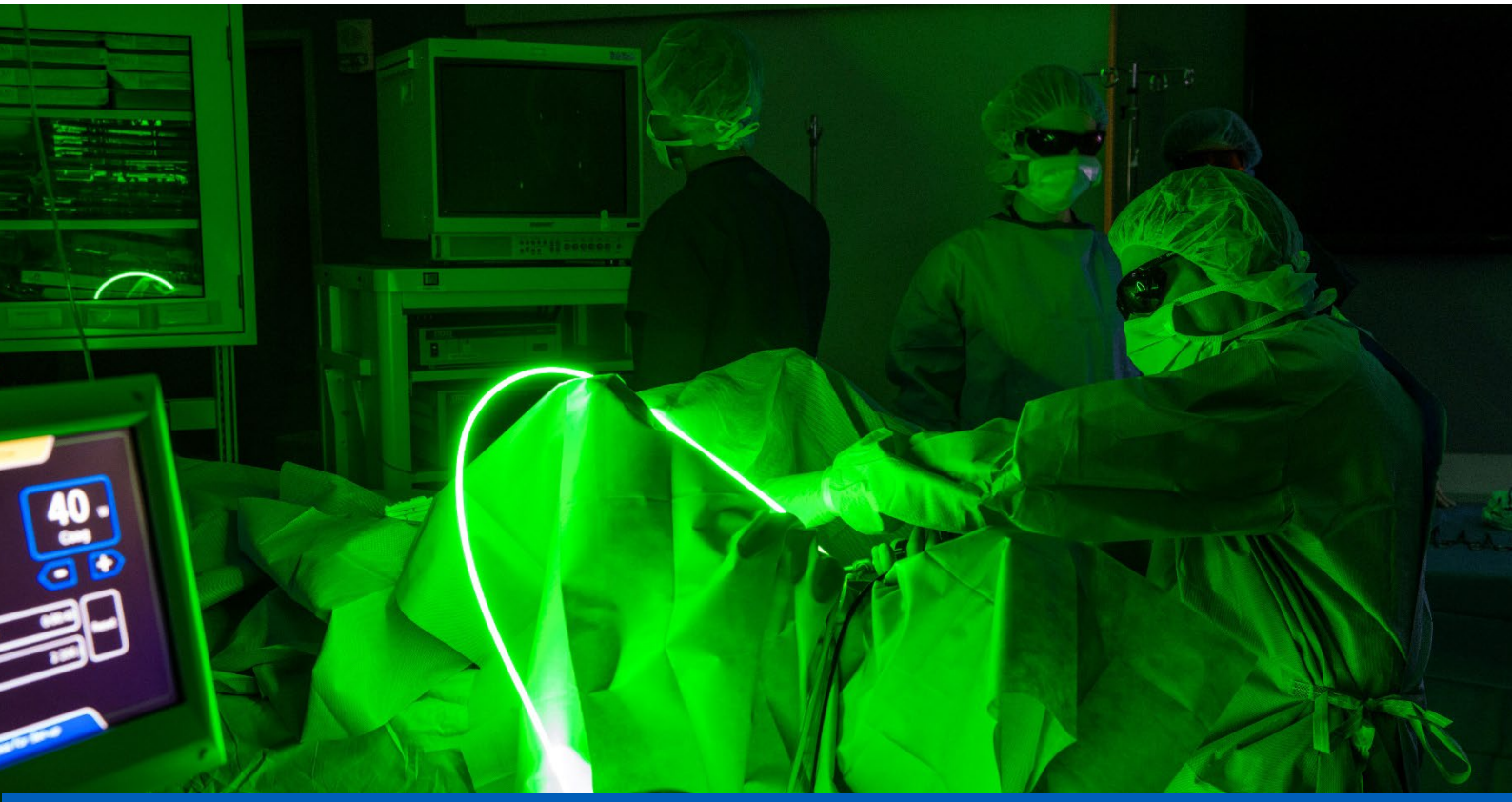
BAUN British Association of Urological Nurses

NHS IMPACT Improving Patient Care Together

Urology: towards better care for patients with bladder outlet obstruction

A practical guide to improving the management of bladder outlet obstruction

January 2022, updated August 2023



GIRFT is part of an aligned set of programmes within NHS England

Executive summary

Who should read this guide?

This work has been conducted with those involved in urology service improvement in mind. Clinicians, operations managers and commissioners should all find useful insights within the document to shed light on how bladder outlet obstruction services can be improved to the benefit of patients and the NHS.

What is the guide's aim?

The guide describes the key features of a contemporary and comprehensive bladder outlet obstruction service and acts as a guide for teams who are committed to high-quality care. It will aid the identification of potential 'gaps' in their current service and offer practical advice that will then help the multi-disciplinary team to bridge them.

What the guide contains:

Case for change

1. Introduction
2. Benefits of improving care for patients diagnosed with bladder outlet obstruction

Good practice bladder outlet obstruction pathway

3. The bladder outlet obstruction pathway
4. Key components of high-quality bladder outlet obstruction care:
    a. Managing patients in a timely manner to improve patient experience and outcomes
    b. Providing a one-stop service for patient assessment to improve quality and increase efficiency
    c. Providing high-quality information to patients
    d. Offering a comprehensive range of treatment options within a urology area network
    e. Maximising the use of day surgery and improved recovery pathways
    f. Optimising arrangements for follow up and audit
    g. Developing a workforce with specific knowledge and skills for managing bladder outflow obstruction

Resources to support service improvement

5. Good practice case studies
6. Additional information
7. Delivery checklist
8. Suggestions for areas of research that would help inform future quality improvement work on bladder outlet obstruction care

Appendix

Full page pathway
Glossary
Contributors

Foreword

The 2018 GIRFT national specialty report on urology demonstrated a wide variation in practice across the NHS and highlighted the need for improvement in urological practice in a range of areas. The GIRFT Best Practice Academy aims to identify good practice and provide guidance on service improvement, particularly focussing on common conditions and frequent interventions, thereby maximising impact.

The starting point in the quality-improvement process is the recognition that some aspects of care are suboptimal. While this is apparent to some of those who are delivering services, the GIRFT methodology of data analysis and clinically-led conversations with front-line staff, which culminated in the publication of the National Specialty Report, definitively demonstrated that we can do better. The next step is to understand where we should be heading. NICE guidance provides the clearest and best-researched evidence that can be used to guide practice. However, inevitably, there are gaps in such guidelines when it comes to defining how first-class clinical services should function. These are filled by expert professional opinion, typically provided to urology by the British Association of Urological Surgeons (BAUS), the British Association of Urological Nurses (BAUN) and the British Association of Day Case Surgery (BADS).

The GIRFT Academy developed this guide on the management of bladder outflow obstruction to support the implementation of good practice. This comes at a time when the management of this common condition is both improving and getting more complex. Patients can now be offered a range of treatment options as effective and safe alternatives to monopolar transurethral resection of the prostate (TURP). There is the added benefit that some of these technologies can be delivered as day cases and, in select cases, as outpatient procedures. All men requiring prostate surgery to treat bladder outflow obstruction should be counselled about their options for treatment, using a patient-centric approach to decision making.

We hope this document will facilitate progress that delivers improved outcomes and experiences for patients with bladder outlet obstruction.

Richard Hindley, *Chair of GIRFT Academy bladder outlet obstruction sub-group and Consultant urologist at Hampshire Hospitals NHS Foundation Trust*

Kieran O'Flynn, *GIRFT co-lead for Urology and Consultant urologist at the Northern Care Alliance NHS Foundation Trust*

John McGrath, *GIRFT co-lead for Urology and Consultant urologist at the Royal Devon and Exeter Foundation Trust*

Simon Harrison, *GIRFT co-lead for Urology and former Consultant urologist at the Mid-Yorkshire Hospitals NHS Trust*

Professor Tim Briggs CBE, *GIRFT Programme Chair and National Director of Clinical Improvement for the NHS.*

About GIRFT and the GIRFT Academy

Getting It Right First Time (GIRFT) is an NHS programme designed to improve the quality of care within the NHS by reducing unwarranted variation. By tackling variation in the way services are delivered across the NHS, and by sharing best practice between trusts, GIRFT identifies changes that will help improve care and patient outcomes, as well as delivering efficiencies such as the reduction of unnecessary procedures and cost savings.

The GIRFT Academy has been established to provide easily accessible materials to support best practice delivery across specialties and adoption of innovations in care.

Importantly, GIRFT Academy is led by frontline clinicians who are expert in the areas they are working on. This means advice is developed by teams with a deep understanding of their discipline, generated by the management of services on a daily basis.

The GIRFT programme is one element of the government's response to the recommendations of Lord Carter's report on operational productivity and performance in NHS acute trusts in England, published in 2016. The Carter Report highlighted the GIRFT programme within its theme on quality and efficiency, outlining the orthopaedic GIRFT pilots which identified the scale of benefit to tackling unwarranted variation.

For more information on the GIRFT programme, visit our website at:

www.gettingitrightfirsttime.co.uk

GIRFT Academy has also published urology delivery guides on:

- **Outpatient transformation**
- **Acute stones**
- **Bladder cancer**
- **Kidney cancer**
- **Urological Investigation Units**
- **Urology Area Networks**
- **Strategic framework for recovery**

These are available at: www.gettingitrightfirsttime.co.uk/urology

1. Introduction

The development of lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH) is a common condition often resulting in a significant adverse impact on quality of life. With advancing age, the prostate enlarges in size, which is often termed benign prostatic enlargement (BPE) thereby obstructing the bladder outlet. Over one third of men aged over 50 in the UK are living with moderate or severe urinary symptoms, which for the majority is due to bladder outflow obstruction (BOO). This equates to 3.4 million men in the UK, and is likely to represent a growing health burden due to an ageing population.

Men presenting with urinary symptoms due to BOO typically have experienced symptoms for many years before seeking help. Following assessment, lifestyle changes and medications are usually first line recommendations. However, a substantial number of men will require surgical treatment, either because of the severity of their condition or because of a failure of conservative treatment to control symptoms. A suite of minimally invasive surgical treatments (MISTs) has built up over recent years, replacing the traditional mainstay of the TURP. This increased range of treatments has meant that there is now a requirement for specialist assessment to include more complex counselling of patients about their options.

By supporting networked urology teams to focus on the opportunities for improvement in their BOO service, we hope to reduce variation in practice and improve patient experience and outcomes. The changing NHS landscape and an increased focus on collaboration means that even the best performing centres should aspire to further improvements.

The timing of this document is particularly relevant given the potential for most of the innovative treatment options to be delivered as day case surgery, or even outpatient treatment. This provides a focus on efficiency and effectiveness that should ensure that patients have access to the right treatment, at the right time and in the right setting, while freeing up NHS resources.

The rapidly changing clinical landscape of BOO management provides interested clinicians with an opportunity to explore this field as a sub-specialty, networking with similarly interested colleagues across the country. This move to sub-specialisation will expedite efforts to drive service improvement.

Further information and context on lower urinary tract symptoms and bladder outlet obstruction are linked to from section 6 of this guide.

2. Benefits of improving care for bladder outlet obstruction patients

As evidenced through the previous GIRFT review of urology services, the case for delivering service improvement across the BOO pathway is strong. The benefits to patients, clinicians and the wider NHS are clear.

A BOO service must be built around the requirements of the individual patient. The treatment portfolio has expanded in such a way as to make it possible to tailor treatment to the specific needs of the patient. This patient-centred approach should drive improvements in patient experience and outcomes, measurable using a wide range of metrics, including hospital stays, readmission rates and retreatment rates.

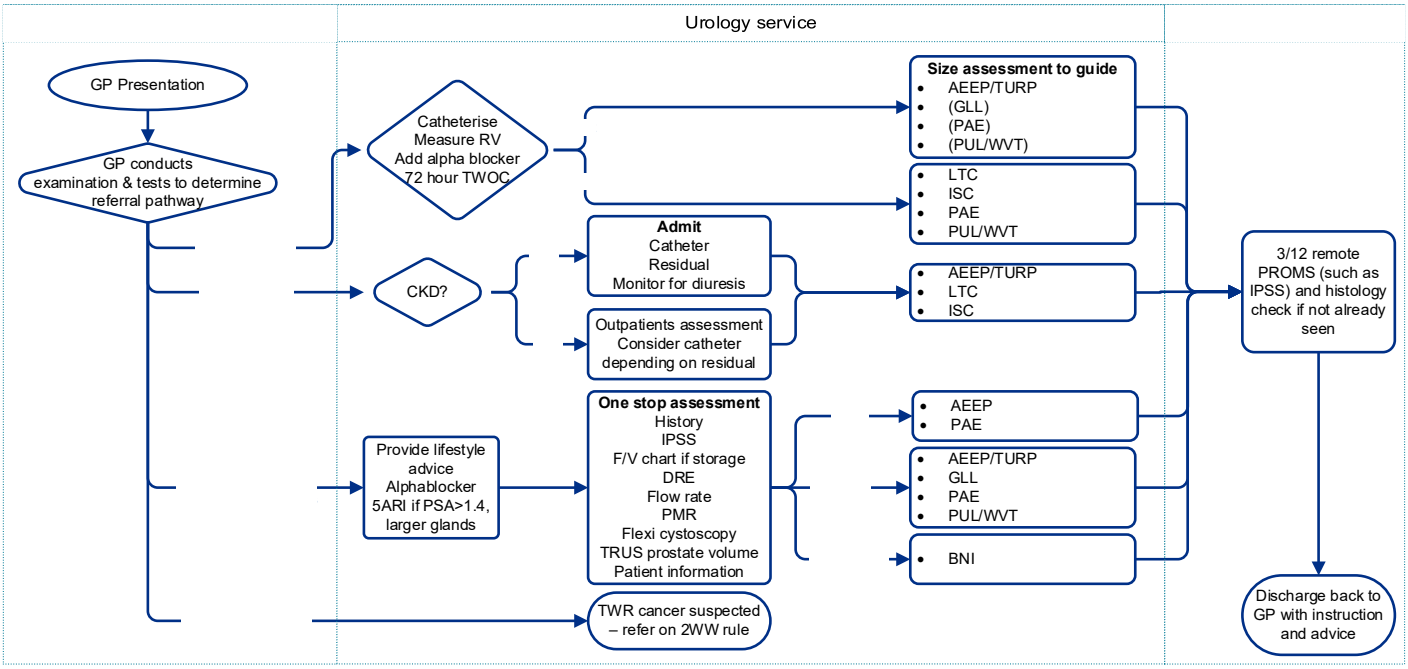
Seeking to deliver appropriate treatments through day surgery, and potentially via outpatients, will often be more convenient and a preferred option for patients. Furthermore, the ability to treat suitable patients as day cases, will reduce pressure on inpatient beds and reduce disruption from cancelled operations. Day case surgery also delivers significant benefits to overall urology services, freeing up operating theatre capacity and optimising waiting list management.

Taking a best practice approach to BOO management has the potential to unlock cost savings for the NHS in other ways. Improved patient outcomes ensure fewer patients experience incontinence and/or sexual disfunction, both of which have a knock-on effect in terms of reducing spend on medicines. A collaborative, network-wide approach to implementing service improvements facilitates the rationalisation and best use of NHS resources across a wider geography. This approach will also enable centres to focus on what they are good at and will provide opportunities for sub-specialisation within the urology team.

3. The bladder outlet obstruction pathway

Summary of the pathway

This pathway covers the various modes of presentation for men with problematic urinary symptoms with an aim not to overcomplicate. The subsequent paragraphs provide a more detailed explanation of the pathway. The glossary at the end of this guide explains the meaning of the various acronyms.



Glossary of pathway terms:

2WW	two-week wait urgent cancer referral	**PDA**	patient decision aid
5ARI	5-alpha-reductase inhibitors	**PMR**	post micturition residual
AEEP	anatomical endoscopic enucleation of the prostate	**PROMS**	patient reported outcome measures
BNI	bladder neck incision	**PSA**	prostate-specific antigen
DRE	digital rectal examination	**PUL**	prostate urethral lift
F/V	urinary frequency / volume chart	**RV**	residual volume
GLL	green light laser	**TRUS**	trans-rectal ultrasound
IPSS	patient satisfaction scores	**TURP**	transurethral resection of the prostate
ISC	intermittent self-catheterisation	**TWOC**	trial without catheter
LTC	long-term use of urinary catheter	**TWR**	two-week referral
PAE	prostate artery embolisation	**WVT**	water vapour therapy

First presentation and initial assessment

The majority of BOO patients present to their GPs with lower urinary tract symptoms (LUTS), such as a reduced urinary stream, urinary urgency or urinary incontinence. Initial assessment and treatment with medication takes place in primary care. Those who fail to respond adequately to first-line treatment will be referred for specialist care.

For men presenting with acute painful retention of urine, it is important to assess the residual urine volume after catheter drainage and to understand the possible triggers for the episode. The majority of patients are treated with an alpha blocker, followed by a trial without catheter (TWOC). Onward referral for assessment by a urologist is recommended:

- if the trial fails or, after a successful TWOC,

- if there are concerns regarding the potential for further retention episodes or ongoing troublesome symptoms. For some patients, the initial TWOC will need to be organised through secondary care services.

People with chronic retention of urine are likely to need hospital assessment because some patients will have associated hydronephrosis and renal impairment.

Urology service

Patients are referred to urology services either as elective outpatients or as emergency cases.

In the outpatient setting, a LUTS one-stop clinic is an ideal forum for assessment and treatment-planning. The dedicated LUTS clinic streamlines clinical assessment, appropriate investigations, patient information and treatment planning. At this visit, patients should be adequately supported using a variety of materials to explore and access the range of treatment options available within the urology area network (UAN). It may be necessary to refer the patient to another hospital or trust for the most appropriate treatment. Key factors for decision-making include the mode of presentation, patient concerns and expectations, comorbidities and the volume of the prostate gland.

For patients presenting with painful acute urinary retention, the immediate need is for bladder drainage in order to relieve pain. Most patients will be suitable for conservative treatment with medication and a planned trial without catheter, carried out either as an outpatient or in the community. However, surgical treatment will be needed for those that fail to re-establish satisfactory micturition and for those in whom a TWOC was contraindicated. Such patients will need to be informed about their treatment options and will choose, with the help of decision-aids, which treatment approach best meets their needs. Treatment may involve a surgical procedure, or conservative, catheter-based management.

Chronic retention patients are at risk of progressive kidney damage. Identifying those who have renal impairment, or are at risk of developing such damage, is a priority. With kidney function safeguarded, chronic retention patients will go forward for either continuing catheter management, with intermittent catheterisation (CISC) or an indwelling catheter, or surgical treatment of their BOO.

If on-going catheterisation is needed for a patient with BOO who is awaiting definitive surgical treatment, CISC should be considered (in appropriately selected cases) as an interim measure, because of the reduced morbidity when compared with a long term in-dwelling catheter. Catheterised patients (or those performing CISC) should be prioritised for surgery and services should be streamlined in an effort to reduce the morbidity associated with prolonged catheterisation. It is expected that functioning urology area networks will organise services in such a way so as to offer prompt treatment to men with catheters or severe symptoms, avoiding waiting times of over 3 months, in line with the GIRFT sentinel metric.

Discharge and follow up

It is important that there are appropriate and efficient pathways in place once treatment of BOO has been undertaken, be it conservative or surgical. Again, this will need to be appropriate to the needs of the individual patient. Good quality patient education and clarity about follow up arrangements will reduce patient anxiety and the numbers of unplanned contacts with NHS services.

Innovation in follow up care should allow a range of options to be available, including face-to-face and virtual consultations. This is an area where patient initiated follow up arrangements may also work well.

4. Delivering improvements in bladder outlet obstruction management

This section of the guide provides detailed consideration of the key areas for quality improvement in bladder outlet obstruction management. Explanatory remarks (aimed particularly at the non-urologist) can be found under each heading, including guidance on what good care might look like. The guidance links to good practice case studies, which can be found in Section 5 of the document, and the additional resources in Section 6.

4A Managing patients in a timely manner to improve patient experience and outcomes

Key quality actions:

- **Ensure that men with severe lower urinary tract symptoms are prioritised in patient pathways**
- **Ensure that urinary retention pathways do not allow inappropriate delays in care to develop**
- **Ensure that patients with indwelling catheters, or severe lower urinary tract symptoms, are afforded a high priority on surgical waiting lists**

There is a large range in symptom severity in men who are referred to secondary care for LUTS management. Within this group, are some with severe symptoms, such as those with urinary incontinence or frequent urinary tract infections. In contrast, many men with LUTS have symptoms that are causing little inconvenience. In an era of relatively long waits for care, it is important that those with severe LUTS are afforded priority in accessing diagnostic and assessment services.

Data captured within the GIRFT programme, and the clinically-led discussions during GIRFT trust visits, have shown that men who present with urinary retention, and go on to need surgical treatment of their BOO, often fail to undergo surgery within a reasonable time interval. It is important that pathways for urinary retention do not build in inappropriate delays. This is a key GIRFT sentinel metric. A key factor is ensuring that the patient has an assessment by a senior decision-maker at an early stage in the pathway, so that inappropriate TWOCs are not attempted, and those who require surgery are placed on the waiting list as soon as the need for surgery is clear. At this point an early referral to an anaesthetic review in pre-operative assessment can help in determining risk profiles for anaesthesia / surgery and guide appropriate treatment modalities for the patient.

For catheterised men awaiting surgery for the relief of acute urinary retention, there is strong evidence supporting early surgery. Within six weeks, a patient with an indwelling catheter will have their urinary tract colonised with bacteria. There is an incidence of catheter-associated urinary tract infection in these men of around 8-10%.The major side-effects reported in a UK study of such men, who were awaiting surgery, were urinary leak (46%), mild haematuria (44%), urgency (42%), pain around the penis (42%), painful erection (31%) and catheter blockage (26%).

In addition to these patient-reported outcomes, there are catheter-associated acute presentations to emergency departments and hospital admissions. The burden of attendances and admissions with catheter-associated UTI, blockages, pain and other symptoms is well-documented.

It is unacceptable for catheterised patients to remain on non-prioritised surgical waiting lists. In the first instance, patients with indwelling catheters should expect to have undergo surgery within 3 months by:

- Actively managing waiting lists, with clear lines of responsibility
- Validating waiting lists with appropriate clinical input and risk-assessment mechanisms
- Supporting patients to make informed decisions with regard to on-going care

Read our case study on timely patient management

4B Providing a one-stop service for patient assessment to improve quality and increase efficiency

Key quality actions:

- **Ensure that protocols are available for primary care colleagues, so that seamless care is provided for men with lower urinary tract symptoms**
- **Establish one-stop clinic services for men with lower urinary tract symptoms**

All symptomatic patients with suspected BOO should be initially assessed and managed in primary care. If symptoms become refractory to treatment, or if side effects are not tolerated, a referral to secondary care is needed. To ensure optimal co-ordination between primary and secondary care, protocols should be in place that set out what care should be provided in primary care, (e.g lifestyle advice and primary medical management), and the triggers for referral to specialist care.

Many innovations have contributed improvements in the care provided to men with LUTS. These include improved methods of assessment, an increase in options for conservative treatment and the development of a number of different operative procedures. Suitability for the different surgical operations depends on factors such as prostate anatomy and size, catheter-dependence, and level of concern about maintaining sexual function. This complexity means that dedicated clinics, run by urologists with a particular interest in BOO management, are needed to ensure that an informed patient is able to navigate a shared decision-making process.

An efficient one-stop service is dependent on excellent communication with patients. Prior to attending, patients need to understand how the clinic works, and complete pre-appointment questionnaires and charts. They need to know what the on-the-day assessment process will involve, and the nature of investigations that might be carried out. Finally, they should have a basic understanding of the causes of LUTS and the treatment options that might be discussed.

The clinic should be configured so that only a small minority of patients fail to complete the assessment process and leave without a clear management plan. Supporting materials should be used to ensure that the patient understands all available options. Future best practice is likely to involve the use of validated patient decision aids. Local knowledge of the available technologies within the UAN is needed in order to inform the decision-making process. Where the chosen treatment is not offered at the local hospital, the patient will need to be entered on the waiting list of the unit where that operation is performed. All of the relevant information about their case should be available in the receiving hospital, so that there is no need to repeat the assessment process.

Read our case studies on one-stop urology clinics

4C Providing high-quality information to patients

Key quality actions:

- **Review the portfolio of patient information that is offered to men with bladder outflow obstruction**
- **Ensure that patient decision-aids are available to facilitate discussions about treatment options**

Accurate, understandable and accessible patient information is vital in modern medicine. Treatment choices for patients with BOO are complex due to the range of possible approaches that can be used. Different techniques will produce subtly different outcomes and implications for patients. Side-effects can be embarrassing for patients to discuss, yet failure to address them can have devastating consequences. Communicating these issues to patients, and being confident that they have understood, is a considerable challenge but is central to the process of informed consent.

Expert input is needed to produce useful patient information resources. For example, one in five adults find it challenging to understand language aimed at a typical 12-year-old, so that the language of written content must be appropriate to the audience. Information should be well presented and engaging. Including pictures and diagrams will help improve patient understanding. Information should be accessible to all, which may require translation into a number of different languages and formats. Centres should look at their own patient demographics to determine local patient information requirements and tailor information accordingly.

Increasingly, patients look online to find their own information. It can be difficult for them to navigate the large quantity of information available and to identify trustworthy sources. Clinicians should be able to offer guidance to patients about getting the best out of online material.

Patient Decision Aids

More recently, a number of patient decision aids (PDAs) have been developed. These go one step further than the provision of information alone, and help patients to make informed choices, taking their personal values and preferences into account. They provide information about available options from an evidence-based perspective, encourage active engagement with the decision-making process and help patients to think through what is important to them, so that they can make choices that reflect their priorities and wishes. A number of PDAs have already been developed for shared decision making in BOO treatment, the most advanced of which is from the Canadian Urological Association, published in May 2021.

Use of a BOO PDA for patients deciding between non-surgical, surgical and minimally invasive treatment options is recommended. Centres should be encouraged to use a PDA even if they are unable to provide all the treatment options locally. It is vital, moving forward with UAN collaboration, that patients have equity of access to all treatments.

Read our case study on understanding patient information requirements

Read about areas for further research in patient decision aids

4D Offering a comprehensive range of treatment options within a urology area network

Key quality actions:

- **Develop collaboration between all of trusts within a Urology Area Network to ensure that a comprehensive range of BOO treatment options is available**
- **Ensure that investment in BOO technology is part of an overall UAN plan that provides an efficient use of resources**
- **Review arrangements for recruitment of patients into BOO clinical trials**

Among the range of NICE approved treatments of bladder outlet obstruction are:

- monopolar or bipolar transurethral resection of the prostate
- transurethral vaporisation of the prostate
- holmium laser enucleation of the prostate
- transurethral incision of the prostate
- water vapour therapy
- prostate artery embolization
- prostatic urethral lift

With an increasing range of new innovations for the treatment of BOO, not all treatment options will be available within a single centre. It is expected that hospitals within a UAN collaborate, so that patients can be offered a range of treatments, even if this means travelling beyond their local centre.

Some procedures, such as prostate artery embolisation (PAE), may be restricted to a small number of centres. This should not limit appropriate patients accessing this treatment but may necessitate more than one UAN referring patients to a particular centre.

Within the UAN, there should be consistency of the use of patient information resources and patient decision aids. Similarly, there needs to be a clear description of the UAN's provision for BOO surgery.

An earlier referral to anaesthetic review in pre-operative assessment can help in determining risk profiles for anaesthesia and surgery, and guide appropriate treatment modalities for the patient.

Evaluation of the results of different treatment modalities for BOO is ongoing as it takes a number of years before mature outcomes can be assessed. It is important that patients should, wherever possible, be offered the option of being recruited into clinical trials that evaluate BOO management.

There is a responsibility on all service providers to use NHS resources efficiently. It is incumbent on clinicians and managers actively to collaborate in developing a UAN plan for BOO treatment that is efficient and effective. This will mean that different hospital sites might offer different treatment options within a system that allows free access for patients to a comprehensive range of therapies.

Read our case study on providing patients access to innovation

Read our guidance on Urology Area Networks

4E Maximising the use of day surgery and improved recovery pathways

Key quality actions:

- **Develop day surgery pathways for BOO patients in line with British Association of Day Surgery guidance**
- **Ensure that any patient who is discharged with a catheter in situ is provided with support, and early catheter removal**

The NHS Plan 2000 suggested that 75% of elective surgery should be performed as day case surgery and the British Association of Day Surgery (BADS) has supported hospitals working towards this goal with its guidelines. However in many places this has yet to be suitably applied for men undergoing BOO surgery. Patient, surgical, anaesthetic and environmental factors have to be taken into account in the implementation of best practice pathways, such as those detailed in the National Day Surgery Delivery Pack.

Traditionally, TURP has been associated with an operative time of 60-90 minutes and a 3-4-day hospital admission. However, the use of green light and holmium lasers for vaporisation or enucleation of the prostate, as well as advances in bipolar TURP (bTURP), have been adopted to reduce blood loss and length of stay following bladder outflow surgery. More recently, the use of newer, minimally-invasive surgeries, including prostatic urethral lift and water vapour therapy, have been introduced. The duration for minimally-invasive procedures is around 20 to 30 minutes and most patients do not need a hospital stay.

As a result of these technical innovations, alongside anaesthetic developments with short acting spinal agents and fast recovery techniques, focus has turned towards the potential for bladder outflow surgery to be performed in a day case setting. This will necessitate investment in equipment and training, given that, currently, 80% of BOO operations are TURPs.

Managing patients' expectations of their treatment pathway is important in maximising day case rates. It is helpful to start this process within a day case specific pre-operative assessment, as recommended in the BADS best practice pathways. Discharge protocols are also integral to successful day surgery. Adherence to a rigorous, nurse-led discharge protocol is known to improve the efficiency of patient discharge.

An important element to ensuring high use of day surgery, or short inpatient stays, is catheter management. Using modern technology, many patients can be discharged on the day of surgery, catheter-free. However, some may need to be discharged with a catheter in situ. It is recognised that pre-operative patient education and post-operative support will allow many patients to be satisfactorily discharged with a urinary catheter in situ. Catheter removal in the early post-operative period can be organised either at home or on return to an outpatient facility.

Read our case study on day case BOO surgery and view an example same-day discharge pathway

It is highly desirable for patients to be able readily to access advice following discharge home. This can be achieved using telephone advice lines and drop-in assessment facilities, should a face-to-face consultation be needed.

4F Optimising arrangements for follow up and audit

Key quality actions:

- **Ensure that follow up arrangements are individualised to the patient and make efficient use of resources**
- **Ensure that the evaluation of key outcome measures is built into follow up protocols**

The landscape of outpatient follow up post-surgical review has changed dramatically over the past few years. In addition to standard face-to-face outpatient clinic appointments, there are virtual appointments, patient initiated follow up (PIFU), and remote monitoring of patient-submitted information.

Follow up after BOO surgery lends itself well to PIFU and remote monitoring, using standardised outcome questionnaires (IPSS, QoL and IIEF scores). Further detail on these approaches can be found in the GIRFT Academy guide to urological outpatient transformation.

Plans for follow up should be clearly communicated to the patient at the time of discharge to make sure that patients know exactly what symptoms or difficulties might arise, and what follow up arrangements are in place. Where patient contact is needed, follow up can be undertaken by specialist nurses or medical staff. Patient contact should be timed to allow early post-operative symptoms to have settled so that any residual longer-lasting symptoms can be evaluated; post-operative follow-up at 3 months is usually appropriate. Follow up arrangements must be robust in relation to the provision of results from histological examination of any prostatic tissue which was sent for analysis.

An important aspect of the after care of patients following BOO surgery is the provision of advice about self-management of residual symptoms. This requires provision of supporting information which give individuals the skills and confidence to treat and cope with their symptoms, while reinforcing their role in taking responsibility for their own health.

A high-quality service for BOO treatment will build the audit of outcomes into its standard practices. Post-operative patient-reported outcome measures are particularly valuable in this type of surgery, given that the majority of patients are undergoing a procedure principally to relieve symptoms.

Read our case study on optimising follow up

4G Developing a workforce with specific knowledge and skills for managing bladder outflow obstruction

Key quality actions:

- **Ensure that patients are managed under the care of consultants who have a special interest in bladder outflow obstruction treatment**
- **Develop the knowledge and skills of the wider clinical team who provide care to bladder outflow obstruction patients**

Whilst it is accepted that there is a need for sub-specialist consultants to undertake certain urological procedures, such as radical prostatectomy and cystectomy, BOO surgery has traditionally been considered a 'general urology' discipline in which all UK urologists have been trained. However, this arrangement is no longer fit for purpose. Many urologists with other sub-specialist interests no longer deliver a consistently high volume of BOO consultations or surgical procedures. With an increasing menu of interventions to choose from, maintaining expertise amongst all consultant urologists is impossible.

It is apparent that BOO management will be undertaken by fewer urologists, and that these consultants will need to have sub-specialist expertise in the field. Identifying this cohort of consultants will need to be undertaken on a UAN basis so that there is a match between capacity and demand across a region. There will need to be changes to urological training to enable clinicians to develop the required sub-specialist skills.

This consultant workforce will need to lead the transition towards a new model of care for BOO patients which delivers the quality ambitions which are set out in the previous sections of this document. This will involve planning for and commissioning the introduction of new technology, designing pathways of care and working with colleagues to develop a suitably skilled multi-disciplinary workforce. Theirs will be a truly transformative agenda.

Read our case study on workforce development

5. Good practice case studies

For each of the seven areas for quality improvement described in section 4 (see above), a number of good practice case studies have been collated. These studies draw on the experience of teams that have already achieved quality improvement in the highlighted area of bladder outlet obstruction.

5A Managing patients in a timely manner to improve patient experience and outcomes

Waiting list management using SMS messaging
University Hospital of Southampton (UHS) NHSFT

Motivation and aims

Backlogs for surgery have lengthened and in urology we have seen BOO surgery waiting lists build alarmingly because of the COVID-19 pandemic. The NHS needs to identify who still needs treatment and how best to prioritise patient flow, making best use of NHS resources. Trusts also need to provide up to date waiting list information to NHS England.

Traditional waiting list management techniques have been resource-hungry, with patients being contacted to check whether they still need surgery, normally via letter. Patients are asked about treatment and are required to phone back to provide the information required. For patients who do not respond, a follow up call would be made. This inefficient way of working leads to delayed data collection and means extra demand is placed on an already overstretched resource.

UHS Digital contacted a trusted tech partner to help them find a more efficient digitalised solution.

What was done

The company took the initial product requirements for a digital waiting list management system from the UHS team and was able to build a minimum viable product within three business days, through use of low-code and iterative, agile working. The solution was presented to UHS Digital and clinicians in a feedback session. The updates and refinements were incorporated in real-time and then released to user acceptance testing. The power of low-code and agile working made it possible to release a solution to go-live within a week.

Mobile details are available for 75% of the 8,500 patients that UHS needs to contact. Now, these patients are sent SMS messages and asked to provide a secure response online. 88% of such patients have interacted with SMS communications. Patients who do not initially respond are sent reminder SMS messages. Letters have been sent out to the 25% of patients who have not provided mobile numbers. Those patients can then access the dedicated website, complete the survey, and provide their mobile number for future use through the digital communications platform.

Successes/ key points of good practice

The system has driven greater efficiencies in patient management, including:

- Instant responses received from patients: the number of responses received on the first day communications are issued via text has exceeded what could be collected within the first few weeks using a traditional, manual approach
- Savings on postage and resource costs are made, compared to sending letters or calling
- Actionable management information is available for the trust
- There has been a significant reduction in the number of calls required to understand patients' waiting list requirements
- NHS England data returns are maximised and returned quickly, with minimal manual input
- Valuable clinical resources can be focused on priority patients

The system has been relatively easy to implement, as it is easy to configure to trust requirements and can be flexibly deployed, with the ability to ask specific questions of patients

Lessons learned

- Agile working has helped deliver a digital solution on a very ambitious timeline
- The system can be adapted and used in many applications

5B Providing a one-stop service for patient assessment to improve quality and increase efficiency

Male lower urinary tract symptoms one stop outpatient clinic
Imperial College London NHS Trust

Motivation and aims

Lower urinary tract symptoms (LUTS) are a substantial reason for referrals to urology clinics across the UK. This places significant pressure on overstretched resources. In the standard (old) pathway at our university hospital, patients waited 20 weeks for a new appointment and 55 weeks for a follow up appointment. Enabling definitive management plans on the same day of the first visit through designing a one-stop LUTS clinic can reduce this 35 week gap.

What was done

As one of Imperial's Flow Coaching Academy quality improvement projects, we introduced a new one-stop male LUTS clinic following a successful pilot.

This new one-stop clinic comprised consultations before and after the required diagnostic tests (flow rate, post-voiding bladder scan, flexible cystoscopies and transrectal ultrasound) on the same day.

This resulted in a definitive management decisions being made on the same day in the large majority of patients.

Successes/ key points of good practice

- The one-stop model reduced the need for follow up appointments from 60% (in the old pathway) to 5%
- The one-stop model increased the number of patients offered surgical management at their first appointment from 10% (old) to 57% (one-stop)
- There was also an increase in discharges from secondary care (from 25% to 32%) at their first consultation
- Patient decisions aids (PDAs) were developed to assist patients in reaching a decision on the most suitable treatment option for their condition

Lessons learned

- Employing a one-stop clinic model for LUTS patients can reduce the patient pathway by 35 weeks, while providing more consistent and higher quality care, and reducing variability in patient management
- Definitive plans regarding surgical management or discharge are made at the first visit, due to the availability of all investigations
- Patient reported satisfaction surveys were positive (98% preferred the one-stop model and 100% were satisfied or extremely satisfied)

One stop BPH clinic

NHS Fife, Scotland (Victoria Hospital Kirkcaldy, St Andrews Community Hospital, St Andrews)

Motivation and aims

A one-stop BPH clinic was introduced to streamline patient assessment and support for BOO surgery, given the large range of options available. The aim was to improve patient experience and develop a more uniform standard of care.

What was done

A one-stop BPH clinic was set up to provide surgical assessment and counselling for BOO patients. Patients are referred to the clinic by GPs (if refractory or intolerant of conservative treatment, or catheterised) or by colleagues if BOO surgery counselling is required. This clinic is run by a consultant urologist with special interest in BOO surgery and supported by a nurse specialist (or dedicated band 5 nurse) who would follow the patients journey and arrange follow up.

Once referred, the booking officer sends the patients a BOO clinic package with a 3 days bladder diary and specific validated questionnaires (IPSS/IIEF3, OAB score, PGI-C score, Retrograde Ejaculation – Y/N, QoL score) for completion prior to attendance. A nurse specialist's contact details are provided for queries.

Upon arrival, a flow rate and post void residual urine volume is measured (unless catheterised). If surgery is recommended, prostate volume estimation is determined with a transrectal probe (unless a recent transabdominal/MRI volume is available). Flexible cystoscopy is performed only if a diagnostic uncertainty is encountered (prostate volume <40 cc, history/flow suggestive of stricture, recent haematuria). The patient will be placed on the waiting list for treatment following their visit to the one-stop clinic and provided with relevant patient information materials.

Nurse-led follow up is provided in the BOO follow up clinic at three months. Validated parameters will be compared and, if concerns are raised, then a consultant led review will be arranged.

Successes/ key points of good practice

- Standardised patient pathways and uniform data collection
- Informed shared decision-making process so that patients are fully informed about their options considering current data, weighing safety/side-effects profile against the likely durability of the treatment
- Patients avoid multiple visits (reduces waiting times)
- Excellent teaching opportunity for trainees/students

Lessons learned

- Patients should be informed that they might be in the unit for a few hours as they will need uroflowmetry, prostate volume, possible flexible cystoscopy, bloods etc
- Ensure 30 minute face-to-face clinic slots are booked
- Easier to set up in a unit that has other one-stop clinic formats
- Counselling should take into account available procedures in the wider UAN, rather than what is only available in the local trust

5C Providing high-quality information to patients

Patient information initiative

BPH Academy, BAUS/GIRFT

Motivation and aims

The project aimed to:

- Formulate a shared decision aid to improve patient understanding of treatment options available for benign prostatic hypertrophy and facilitate their decision-making process
- Provide a standardised template to support discussion and counselling, assisting both the physician/surgeon and patient during this consultation process
- Provide signposting for patients to access additional information
- Standardise representation of information, data and outcomes in a way that is accessible to all patients and in a format that is clear and understandable

What was done

Funding was sourced from BAUS and GIRFT for a patient and public engagement initiative to explore:

- What information participants would like regarding a medical condition that requires treatment (full referral pathway versus focused information on treatment options - along with how comprehensive this information should be)
- At what point in the pathway the information should be provided (ie. at GP appointment or at specialist clinic appointment)
- In what format (paper versus digital) to maximise patient understanding and clear representation of data (engaging infographics)

Successes/ lessons learned

- Patient preferences recorded and now in progress/development
- Standardised animation requested for each procedure accessible by a central locker
- Information required to be engaging with related infographics to represent risk, to ensure understanding by all educational backgrounds
- Acknowledgement that paper patient information is also required
- Digital shared decision tool agreed as an overall preference amongst participants
- The GIRFT Academy BOO team is now engaging with NHS X to progress the development of the decision aid

Key points of good practice

- Ensuring a representative, diverse group of patients helped ensure a balanced approach to materials development
- Circulation of examples of patient information, infographics and animations allowed a tangible review of preferred material
- Enthusiasm of participants to continue the initiative as it develops, allowing continuation of input during the process, helps, demonstrated support for the development of a PDA for BOO

5D Offering a comprehensive range of treatment options within a urology area network

Developing a business case to support the introduction of new technologies

Hampshire Hospitals NHS Foundation Trust (HHFT)

Motivation and aims

Having successfully introduced the prostatic urethral lift (PUL) in early 2016, the business case for introducing another cost saving MIST was relatively straightforward. The predictable fixed cost of only one handpiece per case with water vapour therapy balanced with the avoidance of a TWOC for 82% of patients undergoing PUL left little between the two in terms of financial outlay. The benefits of being able to offer patients a new MIST with the versatility of being able to routinely treat the prostatic median lobe, made this a welcome addition to the portfolio following its introduction in 2017. The goal was to complement the established treatment options and further reduce the demand for inpatient beds and theatre time. An audit performed in 2014 had previously demonstrated an average stay of 19.5 hours for photoselective vaporisation of the prostate and 53 hours for TURP

What was done

In 2017 a business plan was developed and taken through the trust business planning process. Given that we were the first unit in the UK offering this treatment modality, additional governance measures were put in place and a dedicated nurse-led follow up clinic was set up in preparation. A detailed questionnaire was also created which included relevant PROMs, as well as information about urological medications, and objective measures of outcome, including Qmax. A satisfaction questionnaire was included for all patients to complete at six months post operatively. Gland volumes were also recorded. Data was collected prospectively for consecutive patients following the first case in March 2017. The procedure now carries its own reimbursement coding M656 which maps to HRG codes LB70C/D. In 2020, NICE (MTG49) guidance estimated a cost saving of £550 over 4 years compared with TURP.

Successes/ key points of good practice

- Our case series has now exceeded 700 patients treated to date. In the first 4 years pre- and post-operative data is available for the initial 461 patients. We recommend performing the first 15-20 cases under general anaesthetic
- To date, 40% of our patient have had the procedure under GA with the remainder performed under local anaesthetics with or without light sedation. The mean operative time was 17.5 minutes. In an audit period between October 2018 and March 2019, all patients undergoing water vapour therapy on a morning list were discharged the same day. The average length of catheterisation was 5 days. The surgical retreatment rate in the first year was 2.4%.

Lessons learned

- water vapour therapy is a versatile option for men of all ages but is ideally suited to men who wish to preserve sexual function with early return to normal activities
- In light of positive early results, we do consider larger gland sizes >80mls in select cases and the median lobe does not present an obstacle to treatment
- Securing engagement from all members of the urology team can be challenging and can pose a risk to successful adoption of any technology

5E Maximising the use of day surgery and improved recovery pathways

Day Case Holmium Laser Enucleation of the Prostate (HOLEP)
Norfolk & Norwich University Hospital

Growing waiting lists for bladder outflow surgery and limited access to main theatre lists drove a change to day case BOO surgery. In 2012, the option of HOLEP was a one-night stay procedure. A day case pathway was introduced that year with a view to moving this cohort of procedures away from main theatres to free up space for other work.

What was done

Men requiring HOLEP were booked as a day case as default and procedures performed in the day unit from September 2012 onwards. They were discharged with a 3-way catheter (with the irrigation limb spigoted) and a district nurse-led trial of voiding booked for 24 hours. Data for the first two years of the service were audited with three years of follow up.

267 men were performed in the time period. 76.7% were intended as day case procedures.

Successes/ key points of good practice

- 82.9% of intended day case HoLEP patients were successfully discharged the same day
- Readmission rate within 28 days was only 2.94%
- Median post-operative IPSS and quality of life scores were 2 and 0 respectively
- For trusts lacking the scale to deliver HoLEP on site, delivery may be supported via a urology area network

Lessons learned

- The vast majority of HOLEPs regardless of size can be managed as day cases. More than 1200 men have now been managed on this pathway
- Reasons identified for failure of day case discharge included social factors (no accompanying adult at home- 6%), need for continuous bladder irrigation – 5%, and patient being recovered on an inpatient ward rather than day unit
- Sepsis - requiring readmission for intravenous antibiotics was only observed in 1.17% of the cohort
- Spinal anaesthesia was more common in the failed discharge cohort
- The mean age of failed discharge patients was higher

5F Optimising arrangements for follow up and audit

The Follow Up Pathway post minimally invasive surgical treatment

Hampshire Hospitals NHS Foundation Trust (HHFT)

Motivation and aims

Historically, men at HHFT have had the opportunity to access a range of treatments for BOO. When we decided to introduce minimally invasive surgical treatment (MIST), water vapour therapy, at the trust, we decided to set up an additional clinic to ensure that the new patient pathway was optimised. As an early adopter of this technology, we had a responsibility to audit patient experience and outcomes to evidence its impact. Our thorough approach to follow up was intended to provide reassurance on the treatment and guidance on pathway development.

What was done

A post-op BPH telephone clinic was already in place, with patients attending at three months post-op with a view to being discharged to their GP if symptoms had improved.

Initially, follow up for the new post-MIST treatments, prostatic urethral lift and water vapour therapy, was carried out at face-to-face appointments, at three months, six months, 12 months and 24 months. A flow rate and post void residual scan and PROMs IPSS/QOL/IIEF/Ejaculatory score and EQ-5D were completed at each appointment review.

Over time, review of data generated through the intensive follow up schedule, suggested that the frequency and mode of patient follow up could change to a telephone review at three months; face-to-face appointment at six months and a telephone appointment and discharge at 12 months.

Successes/ lessons learned

- MIST treatments are different to traditional operations and necessitate a more patient-centric and collaborative approach to follow up to optimise outcomes
- The introduction of nurse-led review clinics has continued to provide an excellent yet efficient service for patients undergoing BOO treatments
- The evolution of these follow up arrangements has helped inform requirements around future clinics and increased clinical nurse specialist capacity for the BOO service, with the addition of a band 6 and band 4 role
- More sophisticated methods for follow up will be adopted as the service continues to evolve, including patient initiated follow up
- The My Medical records arm set up for BOO in its infancy required additional work to make it fit for purpose. An upgrade will enable patients to upload symptom score values, which will either trigger a red flag to contact the patient or confirm the existing patient initiated follow up pathway. We will also be able to produce reports to evaluate all BOO outcomes, improving out virtual outpatient review

Key points of good practice

- With the review of outpatient utilisation, we were able to sustain the nurse-led clinical follow up for BOO patients
- With data to illustrate the volume of patients for review, we were able to increase the clinical nurse specialist hours for the benign service, to ensure that it was adequately staffed
- PROMs recorded at each outpatient review enabled the department to evaluate surgical outcomes

5G Developing a workforce with specific knowledge and skills for managing bladder outflow obstruction

Streamlining the pathway for men with urinary retention

Freeman Hospital, Newcastle upon Tyne

Motivation and aims

The aim of this service was to streamline the pathway for men with acute urinary retention, from the point of a referral being received to outcome from trial without catheter (TWOC). The service limits the patient to one visit to the hospital but ensures a history has been taken prior to the visit, and that suitable medical management is started, where appropriate, before attending for TWOC.

The motivation for setting up the service was to have a robust, standardised pathway that would increase capacity for men to be seen in the shortest time possible after going into retention, whilst providing opportunities for nurses to upskill. The service started before COVID-19 and used a nurse-led telemedicine assessment at the outset of the pathway, allowing for both on and off site working. We were aware of multiple pathways for patients in retention and wanted to amalgamate these, so that patients received the same standard of care. By enabling three specialist nurses to run the service, we planned to remove variation that could be detrimental to the speed with which patients were seen and assessed.

What was done

We notified all secretaries, doctors (A and E and hospital) and specialist nurses who receive retention referrals to forward these to the TWOC clinic nurses. In addition, patients booked into our consultant hot on-call clinic were diverted to the TWOC clinic.

Dedicated training was delivered to the nurses involved with regards rectal examination and assessment. The nurses involved also shadowed consultant consultations for men in retention, to develop a broader knowledge base on management options and assessment. Time in the nurses' job plans was secured for the initial telephone consultation and production of a letter, generated electronically in real time, which was sent to the patient and their GP.

At the end of the initial consultation, if the plan is for TWOC, the date and time for the TWOC is given to the patient both verbally and in the outcome letter. The TWOC appointment is delivered in a dedicated area set out as a lounge with sofas and soft chairs. At the time of TWOC, men have a rectal examination to exclude a malignant-feeling prostate. In those men who fail and are progressing to surgery, a trans rectal volume scan is performed at that time, if possible. We are continuing to train the specialist nurses so all can perform trans rectal ultrasound volume assessment independently.

Successes/ lessons learned

- Nurses delivering the service enjoy it and actively promote it
- Dedicating time and resources to training and skills development improves staff retention
- Lessons learned:
  - Nurse lead prescribing decreases primary care workload
  - Currently telephone only and no video consultation
  - No patient user group input as yet but a patient feedback exercise will be the next step
  - Some patients may request community-based TWOC and we are considering how best to achieve this and also perform the rectal examination of the prostate

Key points of good practice

- We have amalgamated many points of entry into our service into one pathway, increasing efficiency and patient experience
- Patient booking, delivery and administration is all done by the nurses delivering the service, allowing ownership and a focused approach to service-improvement
- New skills in patient assessment and ultrasound scanning have improved the skills base for nurses within the department
- Telephone initial contact is COVID-19 safe, efficient and allows off site delivery of this part of the service when team members cannot work on site
- Dedicate TWOC lounge aids patient comfort away from a more clinical setting
- Men with no prior LUTS and successful TWOC are discharged to primary care

6. Additional information

Background and context on bladder outlet obstruction

Recommended document	Author	Overview
NICE Clinical Guideline: [CG97] Lower urinary tract symptoms in men: management	NICE	The NICE guideline covers managing lower urinary tract symptoms (LUTS) in men over 18. This guideline was last update in 2010 and is due to be reviewed.
The management of lower urinary tract symptoms in men	Jonathan Rees, Matthew Bultitude, Ben Challacombe	BMJ clinical review article describing management of lower urinary tract symptoms in men, published June 2014
Burden of male lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) – focus on the UK	Mark Speakman, Roger Kirby, Scott Doyle, Chris Ioannou	BJU International review, published March 2014
Comparative efficacy and safety of new surgical treatments for benign prostatic hyperplasia: systematic review and network meta-analysis	Huang et. Al	BMJ research article, published September 2019
The influence of family history on prostate cancer risk: implications for clinical management	Stephen Madersbacher et. Al	BJU International article, published December 2010

Overarching guidance on bladder outlet obstruction management

Recommended document	Author	Overview
EAU Guidelines on the Assessment of Non-neurogenic Male Lower Urinary Tract Symptoms including Benign Prostatic Obstruction	European Association of Urology	EAU guidelines on BPO
AUA Guideline: Management of Benign Prostatic Hyperplasia (BPH)	American Urological Association	AUA guidelines on BPH

6A Managing patients in a timely manner to improve patient experience and outcomes

Recommended document	Author	Overview
Healthcare-associated urinary tract infections in patients with a urinary catheter: Risk factors, microbiological characteristics and patterns of antibiotic resistance	Jimenez et al	Assessment of catheter-associated urinary tract infections in a urology department
Does length of time spent on the waiting list for TURP influence the outcome?	Journal of Clinical Urology	A study to understand whether increasing time on a waiting list influences the outcome from a transurethral resection of prostate

6B Providing a one-stop service for patient assessment to improve quality and increase efficiency

Recommended document	Author	Overview
A framework for re-establishing and developing urology services in the COVID-19 era	GIRFT	Reviews how service recovery might be achieved in urology, including consideration of one-stop clinics
Patient information leaflet for one-stop LUTS clinic	East Sussex Healthcare	Patient information regarding a one-stop LUTS clinic
A novel one-stop LUTS clinic model	Uma Walters Tara Latimer, Sophie Dean, Michael Morgan, Viren Jeram, Tamer El-Husseiny	An abstract from World Congress of Endourology 2019, setting out one-stop clinical model from Charing Cross Hospital, Imperial College Healthcare NHS Trust

6C Providing high-quality information to patients

Recommended document	Author	Overview
Enlarged prostate patient decision aid	Canadian Urological Association	Patient decision aid to discuss surgical treatments for an enlarged prostate
An introduction to patient decision aids	British Medical Journal	Overview of patient decision aid related considerations
NHS Choices information on consent to treatment	NHS Choices	Information on consent and the importance of appropriate written language to the audience and including pictures and diagrams to improve patient understanding.
Insights into the decision-making process for men selecting therapy for non-neurogenic Lower Urinary Tract Symptoms	Winchester Healthy Lives Research Group, Husted, M., Gray, D., Golding, S. E., & Hindley, R.	Qualitative study interviewing male patients to understand the key factors and influences for men when trying to decide between the various treatment options for non-cancerous urinary problems.

6D Offering a comprehensive range of treatment options within a urology area network

Recommended document	Author	Overview
GIRFT Urology: Guide to Urology Area Networks	GIRFT	Based on the experiences of existing UANs, this guide supports urology departments who are planning to establish a network or seeking to improve their existing network.
Contemporary surgical management of benign prostatic obstruction: does there remain a place in the toolbox for TURP?	Journal of Clinical Urology, Trail et al	Overview of treatment pathway considering TURP and newer treatments for BOO
Minimally invasive surgery for benign prostatic obstruction: new insights and future technical standards	Current Opinion Urology, Rijo et al	Review of MISTs

6E Maximising the use of day surgery and improved recovery pathways

Recommended document	Author	Overview
National day surgery delivery pack	GIRFT, BADS, CPOC	A pack designed to enable NHS Trusts to expand and increase day case surgery for the benefit of the patient and the wider healthcare system. Includes case studies on BOO
National day case surgery appendices	GIRFT	Resources to support day case surgery delivery, including 'How to' guides on day case Green Light laser prostatectomy (p26) and day case transurethral resection of prostate (p30)
Guidelines for day-case surgery 2019	Bailey, C.R., Ahuja, M., Bartholomew, K., Bew, S., Forbes, L., Lipp, A., Montgomery, J., Russon, K., Potparic, O. and Stocker, M.	Guidelines from the Association of Anaesthetists and the British Association of Day Surgery
Same-day discharge Bladder Outflow Obstruction surgery pathway	NHS England London Region	A detailed pathway diagram for same-day discharge for bladder outflow obstruction surgery has been developed by the NHS England London Region. The pathway is accompanied by a top-tips document to support implementation.

6F Optimising arrangements for follow up and audit

Recommended document	Author	Overview
UK National Bladder Outflow Obstruction Surgery Snapshot Audit	British Journal of Urology, JJ Anning et al	Study to determine the pre-operative assessment and peri-operative outcomes of men undergoing BOO surgery in the United Kingdom
Current process and outcomes of the surgical management of LUTS due to benign prostatic enlargement: how consistent are we?	Scottish Medical Journal, Joshi et al	Results from the multi-institutional audit of surgical management of BPE in the United Kingdom

6G Developing a workforce with specific knowledge and skills for managing bladder outflow obstruction

Recommended document	Author	Overview
Implementation of a nurse-led LUTS clinic reduces general urology clinic workload in a Model 4 Hospital. Richard to complete	Kevin G. Keane, Mohammud Shakeel Inder, Caroline McIntyre, Shawgi Omer, Elizabeth McEvoy, Et al.	Irish Journal of Medical Science article on a pilot study in Tallaght University Hospital, which found that introduction of a specialist nurse-led clinic significantly reduced the number of patients requiring follow-up in general urology clinics, representing a quality improvement in service provision.

7. Delivery checklist

Pathway component	Key actions
7A Managing patients in a timely manner to improve patient experience and outcomes	• Ensure that men with severe lower urinary tract symptoms are prioritised in patient pathways • Ensure that urinary retention pathways do not allow inappropriate delays in care to develop • Ensure that patients with indwelling catheters, or severe lower urinary tract symptoms, are afforded a high priority on surgical waiting lists
7B Importance of high-quality patient information for BPH patients	• Ensure that protocols are available for primary care colleagues, so that seamless care is provided for men with lower urinary tract symptoms • Establish one-stop clinic services for men with lower urinary tract symptoms
7C Patients being offered the full range of treatment options as part of a urology area network	• Review the portfolio of patient information that is offered to men with bladder outflow obstruction • Ensure that patient decision-aids are available to facilitate discussions about treatment options
7D Providing a one-stop service for patient assessment to increase efficiency, improve quality and reduce demands on patients	• Develop collaboration between all of the trusts within a Urology Area Network to ensure that a comprehensive range of BOO treatment options is available. • Ensure that investment in BOO technology is part of an overall UAN plan that provides an efficient use of resources • Review arrangements for recruitment of patients into BOO clinical trials
7E To introduce PIFU where appropriate but ensure ongoing collection and review of PROMs (IPSS and QoL)	• Develop day surgery pathways for BOO patients in line with British Association of Day Surgery guidance • Ensure that any patient who is discharged with a catheter in situ is provided with support, and early catheter removal
7F In line with BADS recommendations, centres should aim to discharge patients on the same day	• Ensure that follow up arrangements are individualised to the patient and make efficient use of resources • Ensure that the evaluation of key outcome measures are built into follow up protocols
7G Take a comprehensive approach to managing waiting lists	• Ensure that patients are managed under the care of consultants who have a special interest in bladder outflow obstruction treatment • Develop the knowledge and skills of the wider clinical team who provide care to bladder outflow obstruction patients

8. Areas for further research

For those wishing to carry out additional research, the following priorities could help drive further improvements to bladder outlet obstruction care:

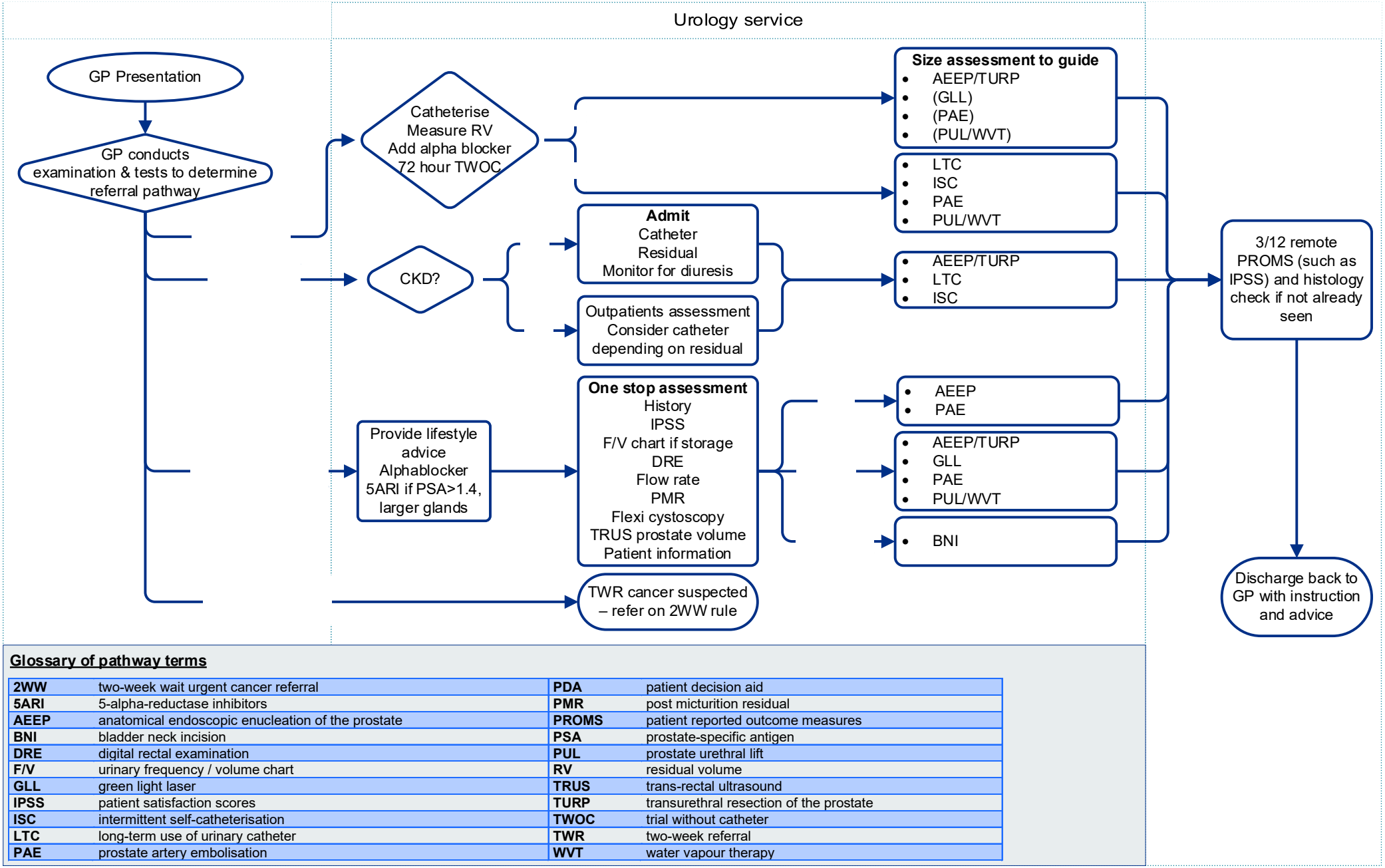
- To evaluate further the optimal patient decision aid for UK men considering treatment options for symptomatic BOO
- To develop and evaluate the feasibility of an intervention that will support clinicians and patients in moving from the 'risk-benefit' part of the treatment option discussion to the 'this is the right treatment for me' part of the discussion
- Randomised trials comparing minimally invasive interventions for the treatment of symptomatic BOO with conventional treatments, including laser therapies and TURP
- To support patients having rapid treatment it would be helpful to have data on what happens to people left with catheters for long periods of time
- Evaluation of new technologies and their use in the UK, including comparison with established treatments
- Further research into the potential role of simulation in training on improving patient outcomes

In developing section 4C on providing high-quality information to patients, it became clear that patient decision aids would be the next step, providing not just information but helping patients to make informed choices by actively engaging them with the evidence and their personal values and preferences.

Clare Bent and Rachel Morrison, members of the GIRFT Academy bladder outlet obstruction group, had begun work on patient decision aids with the support of Margaret Husted and Debra Gray of the University of Winchester Healthy Lives Research Group (HLRG) and Helen Allen and Louise Ward from the Bournemouth University Clinical Research Unit.

It is expected that this work will lead to the development of a patient decision aid product and this will be included in an updated edition of this document and on the GIRFT Academy.

Appendix – Full page pathway

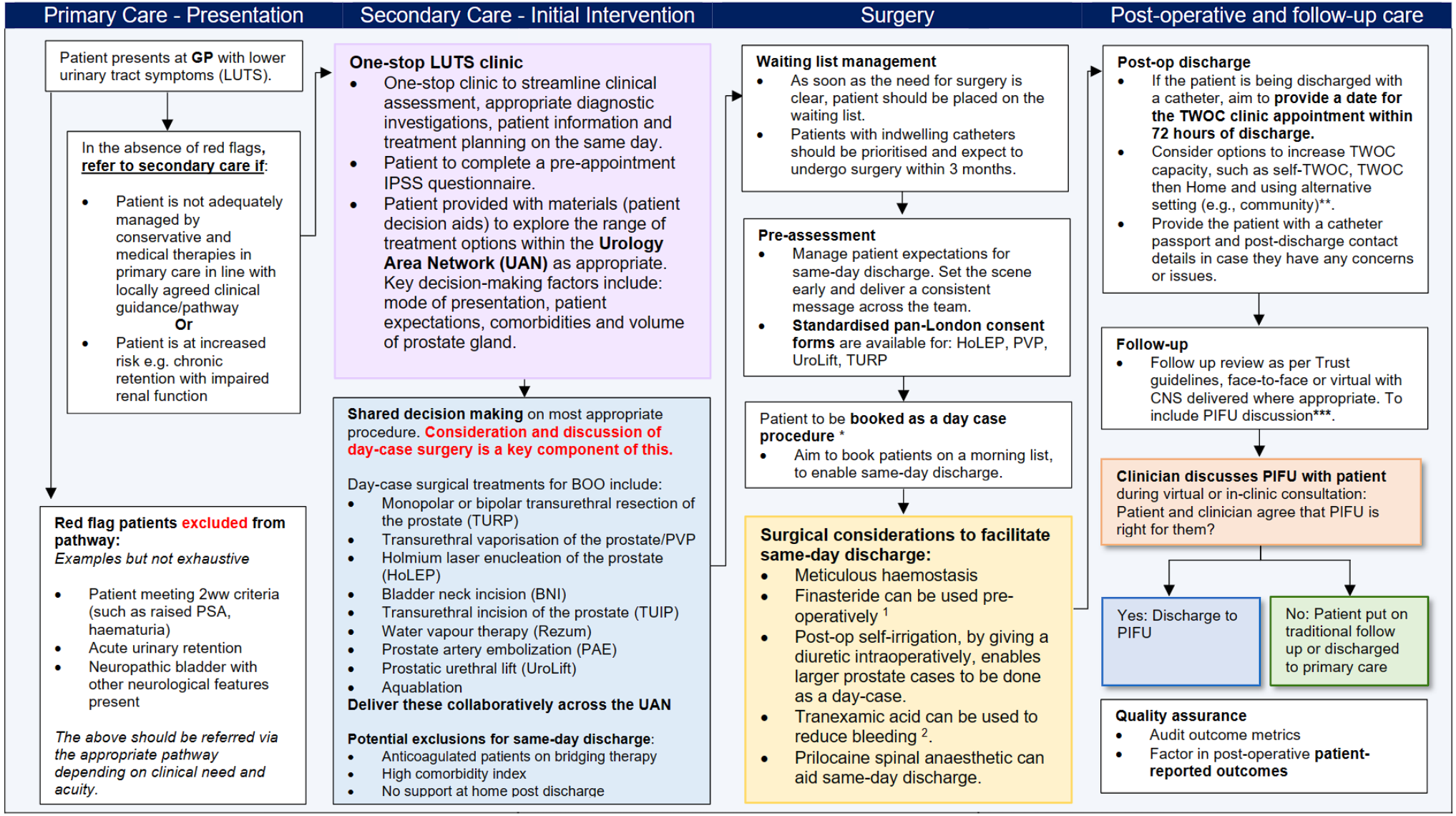


Glossary of pathway terms

2WW	two-week wait urgent cancer referral	**PDA**	patient decision aid
5ARI	5-alpha-reductase inhibitors	**PMR**	post micturition residual
AEEP	anatomical endoscopic enucleation of the prostate	**PROMS**	patient reported outcome measures
BNI	bladder neck incision	**PSA**	prostate-specific antigen
DRE	digital rectal examination	**PUL**	prostate urethral lift
F/V	urinary frequency / volume chart	**RV**	residual volume
GLL	green light laser	**TRUS**	trans-rectal ultrasound
IPSS	patient satisfaction scores	**TURP**	transurethral resection of the prostate
ISC	intermittent self-catheterisation	**TWOC**	trial without catheter
LTC	long-term use of urinary catheter	**TWR**	two-week referral
PAE	prostate artery embolisation	**WVT**	water vapour therapy

Received from Mark Haynes on 03/11/2023. Annotated by the Urology Services Inquiry.

Example same-day discharge BOO surgery pathway from London



*If treated in main theatres due to lack of day-case space, ensure patients are booked and coded as a day-case.
** Guidance on Self-TWOC and TWO then Home is available on FutureNHS here. https://future.nhs.uk/LondonESRTHVLC/view?objectID=39560432
*** Full PIFU Guidance and SOP is available on FutureNHS here. https://future.nhs.uk/LondonESRTHVLC/view?objectId=40257488

Available for download from FutureNHS.

Top tips for implementing the same-day discharge Bladder Outflow Obstruction surgery pathway

One-stop LUTS clinic

- GIRFT recommendation and best practice.
- Information must be accessible and engaging to support patients to make the right choice for them.
- Patient decision aids should be available to support patient decision making.
- Considerations; patient history, urinary frequency/volume chart, IPSS questionnaire, digital rectal examination, flow rate, post micturition residual, flexi cystoscopy, trans-rectal ultrasound prostate volume, patient information.

Surgical considerations

- Leading units in the UK have significantly improved their day case rates by using standard and readily available equipment (bipolar technology), which is good at stopping bleeding and enabling meticulous haemostasis.
- There is good evidence for using finasteride pre-operatively[1].
- Tranexamic acid can be used to reduce bleeding and furosemide to encourage auto irrigation [2,3].
- Post-op self-irrigation means you can do a larger prostate as a day case using diuretics such as furosemide to encourage auto irrigation.
- Prilocaine spinal anaesthetic can aid with same-day discharge.
- Thorough wash out at the end of the procedure to remove chips.

Decision making / Patient criteria

- Shared decision making is essential to enable patients the choice of which procedure is right for them and avoiding surgeon prejudice.
- Information should be available for patients on the types of procedures available in the Urology Area Network (UAN). ICSs are recommended to offer all BOO procedures across the UAN and work collaboratively within the system to deliver BOO surgery.
- Day case is suitable for patients up to stable ASA3 and patients with diabetes [4].

Discharge

- If a patient is discharged with a catheter, they should be given a catheter passport and a TWOC clinic appointment or information for self-TWOC or TWOC then Home (TWOC Services webinar available on FutureNHS)[7].
- Patients should be provided with contact details of who to contact if they have any issues or concerns post-discharge.
- Patients must have support at home post-discharge or be appropriate for the No-One At Home (NOAH) policy.
- PIFU Guidance is available on FutureNHS.

Pre-operative Assessment / Booking

- Ensure patients are pre-assessed and fully understand the implications of a day-case pathway.
- Aim to book patients on a **morning list** to enable enough time for same-day discharge.
- Aim to review the pathway mapping regularly and reflect patient feedback.
- Consider including the prostate gland volume in booking notes to aid scheduling.

Communication

- Ensure patients receive a consistent day-case message throughout the pathway from all members of the team.
- Departmental teaching is essential to ensure consistent messaging and understanding of the pathway.

Oversight

- Utilise Model Health System and National Consultant Information Programme (NCIP) data to monitor progress and consider multiple metrics (including readmission rates).
- Collect and reflect on patient and staff feedback.
- Regular presentation at audit meetings helps to maintain oversight of the pathway.

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6. NHSE London: Same-day discharge Bladder Outflow Obstruction Surgery Learning Event. Webinar recording available on FutureNHS. BOO Surgery - Urology Masterclass - FutureNHS Collaboration Platform
7. NHSE London: TWOC Services: Sharing Innovation Learning Event. Webinar recording available on FutureNHS. TWOC Services: Sharing Innovation - FutureNHS Collaboration Platform

Glossary

Organisations/groups

AUA	American Urological Association
BADS	British Association of Day Surgery
BAUN	British Association of Urological Nurses
BAUS	British Association of Urological Surgeons
EAU	European Association for Urology
GIRFT	Getting it right first time programme

Acronyms

AEEP	anatomical endoscopic enucleation of the prostate
BPE	benign prostatic enlargement
BPH	benign prostatic hyperplasia
CISC	intermittent catheterisation
IPSS, QoL and IIEF	patient satisfaction scores
LUTS	lower urinary tract symptoms
BOO	bladder outlet obstruction
bTURP	bipolar transurethral resection of the prostate
MIST	minimally invasive surgical treatment
PDA	patient decision aid
PIFU	patient initiated follow up
PAE	prostate artery embolisation
PUL	prostatic urethral lift
PVP	photoselective vaporisation of the prostate
TURP	transurethral resection of the prostate
TWOC	trial without catheter
UTI	urinary tract infection
UAN	urology area network
WVT	water vapour therapy or water vapourisation

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EAU Guidelines on

Non-Neurogenic Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO)

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European Association of Urology

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1. INTRODUCTION

1.1 Aim and objectives

Lower urinary tract symptoms (LUTS) are a common complaint in adult men with a major impact on quality of life (QoL) and have a substantial economic burden. The present Guidelines offer practical evidence-based guidance on the assessment and treatment of men aged 40 years or older with various non-neurogenic benign forms of LUTS. The understanding of the lower urinary tract (LUT) as a functional unit, and the multifactorial aetiology of associated symptoms, means that LUTS now constitute the main focus, rather than the former emphasis on Benign Prostatic Hyperplasia (BPH). The term BPH is now regarded as inappropriate as it is Benign Prostatic Obstruction (BPO) that is treated if the obstruction is a significant cause of a man's LUTS. It must be emphasised that clinical guidelines present the best evidence available to the experts. However, following guideline recommendations will not necessarily result in the best outcome. Guidelines can never replace clinical expertise when making treatment decisions for individual patients, but rather help to focus decisions - also taking personal values and preferences/individual circumstances of patients into account. Guidelines are not mandates and do not purport to be a legal standard of care.

1.2 Panel composition

The EAU Non-neurogenic Male LUTS Guidelines Panel consists of an international group of experts with urological and clinical epidemiological backgrounds. All experts involved in the production of this document have submitted potential conflict of interest statements which can be viewed on the EAU website Uroweb: http://uroweb.org/guideline/treatment-of-non-neurogenic-male-luts/.

1.3 Available publications

A quick reference document, the Pocket Guidelines, is available in print and on the Uroweb website. These are abridged versions, which may require consultation together with the full text version. All documents are accessible through the EAU website Uroweb: http://www.uroweb.org/guideline/treatment-of-non-neurogenic-male-luts/.

1.4 Publication history

The Non-Neurogenic Male LUTS Guidelines was first published in 2000. Standard procedure for EAU Guidelines includes an annual assessment of newly published literature in the field to guide future updates.

2. METHODS

2.1 Introduction

For the 2023 Non-Neurogenic Male LUTS Guidelines, a forensic review and restructure of Section 5.3 - Surgical treatment, was undertaken. An assessment of all newly published literature will be performed for the 2024 Non-Neurogenic Male LUTS Guidelines.

Detailed search strategies for the 2022 guideline update are available online:
http://www.uroweb.org/guideline/treatment-of-non-neurogenic-male-luts/supplementary-material.

For each recommendation within the guidelines there is an accompanying online strength rating form which includes the assessment of the benefit to harms ratio and patients 'preferences for each recommendation. The strength rating forms draws on the guiding principles of the GRADE methodology but do not purport to be GRADE [1, 2]. Each strength rating form addresses a number of key elements namely:

1. the overall quality of the evidence which exists for the recommendation, references used in this text are graded according to a classification system modified from the Oxford Centre for Evidence-Based Medicine Levels of Evidence [3];
2. the magnitude of the effect (individual or combined effects);
3. the certainty of the results (precision, consistency, heterogeneity and other statistical or study related factors);
4. the balance between desirable and undesirable outcomes;
5. the impact of patient values and preferences on the intervention;
6. the certainty of those patient values and preferences.

These key elements are the basis which panels use to define the strength rating of each recommendation. The strength of each recommendation is represented by the words 'strong' or 'weak' [4]. The strength of each

recommendation is determined by the balance between desirable and undesirable consequences of alternative management strategies, the quality of the evidence (including certainty of estimates), and nature and variability of patient values and preferences.

Additional information can be found in the general Methodology section of this print, and online at the EAU website; http://www.uroweb.org/guideline/. A list of associations endorsing the EAU Guidelines can also be viewed online at the above address.

2.2 Review

The Non-Neurogenic Male LUTS Guidelines were peer reviewed prior to publication in 2016. The newly added section on management of urinary incontinence in males was peer reviewed prior to the publication in 2022.

2.3 Patients to whom the guidelines apply

Recommendations apply to men aged 40 years or older who seek professional help for LUTS in various non-neurogenic and non-malignant conditions such as BPO, detrusor overactivity (DO)/overactive bladder (OAB), or nocturnal polyuria (NP). Men with other associated factors relevant to LUT disease (e.g., concomitant neurological diseases, young age, prior LUT disease or surgery) usually require a more extensive work-up, which is not covered in these Guidelines, but may include several tests mentioned in the following sections. EAU Guidelines on Neuro-Urology, Urological Infections, Urolithiasis, or malignant diseases of the LUT have been developed by other EAU Guidelines Panels and are available online: www.uroweb.org/guidelines/.

3. EPIDEMIOLOGY, AETIOLOGY AND PATHOPHYSIOLOGY

Lower urinary tract symptoms can be divided into storage, voiding, and post-micturition symptoms [5], and they are prevalent, cause bother and impair QoL [6-9]. An increasing awareness of LUTS and storage symptoms in particular, is warranted to discuss management options that could increase QoL [10]. Lower urinary tract symptoms are strongly associated with ageing [6, 7], associated costs and burden are therefore likely to increase with future demographic changes [7, 11]. Lower urinary tract symptoms are also associated with a number of modifiable risk factors, suggesting potential targets for prevention (e.g. metabolic syndrome) [12]. In addition, men with moderate-to-severe LUTS may have an increased risk of major adverse cardiac events [13].

Most elderly men have at least one LUTS [7]; however, symptoms are often mild or not very bothersome [9, 10, 14]. Lower urinary tract symptoms can progress dynamically: for some individuals LUTS persist and progress over long time periods, and for others they remit [7]. Lower urinary tract symptoms have traditionally been related to bladder outlet obstruction (BOO), most frequently when histological BPH progresses through benign prostatic enlargement (BPE) to BPO [5, 8]. However, increasing numbers of studies have shown that LUTS are often unrelated to the prostate [7, 15]. Bladder dysfunction may also cause LUTS, including detrusor overactivity/OAB, detrusor underactivity (DU)/underactive bladder (UAB), as well as other structural or functional abnormalities of the urinary tract and its surrounding tissues [15]. Prostatic inflammation also appears to play a role in BPH pathogenesis and progression [16, 17]. In addition, many non-urological conditions also contribute to urinary symptoms, especially nocturia [7].

The definitions of the most common conditions related to male LUTS are presented below:

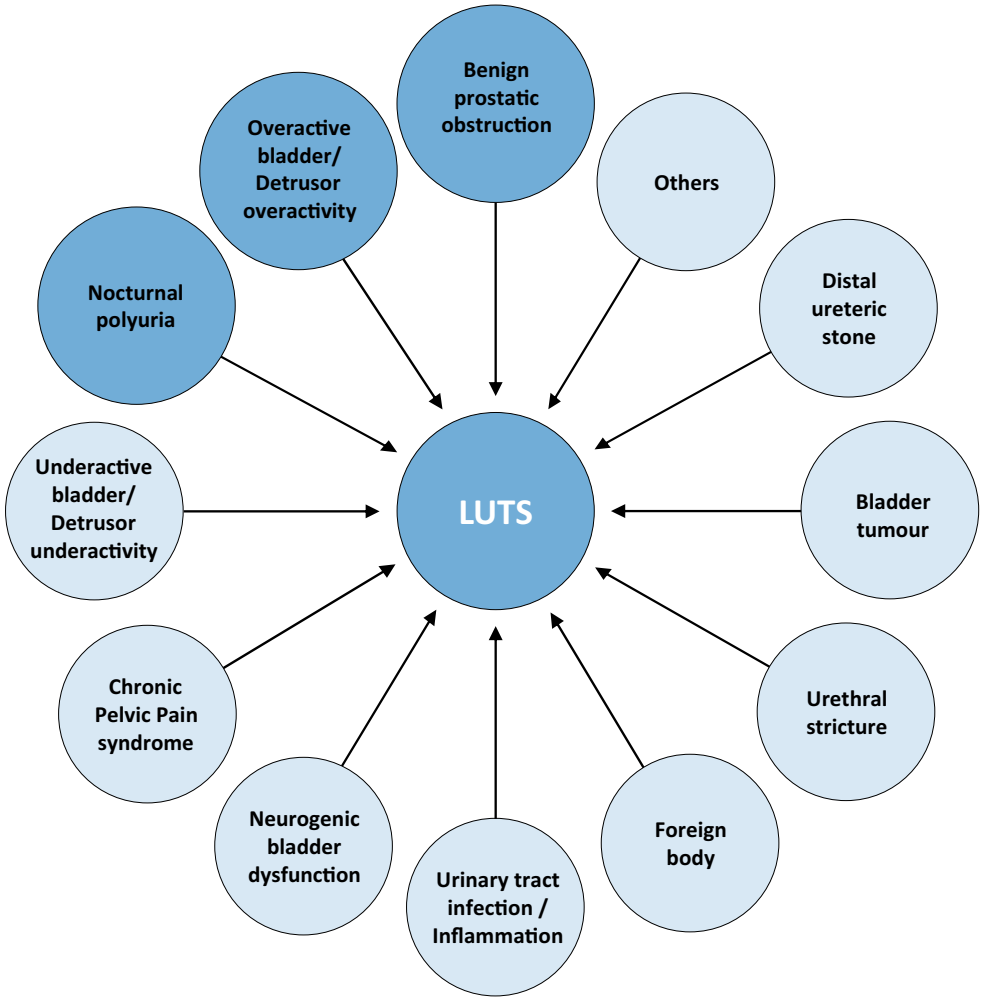
- Acute retention of urine is defined as a painful, palpable or percussible bladder, when the patient is unable to pass any urine [5].
- Chronic retention of urine is defined as a non-painful bladder, which remains palpable or percussible after the patient has passed urine. Such patients may be incontinent [5].
- Bladder outlet obstruction is the generic term for obstruction during voiding and is characterised by increasing detrusor pressure and reduced urine flow rate. It is usually diagnosed by studying the synchronous values of flow-rate and detrusor pressure [5].
- Benign prostatic obstruction is a form of BOO and may be diagnosed when the cause of outlet obstruction is known to be BPE [5]. In the Guidelines the term BPO or BOO is used as reported by the original studies.
- Benign prostatic hyperplasia is a term used (and reserved) for the typical histological pattern, which defines the disease.
- Detrusor overactivity is a urodynamic observation characterised by involuntary detrusor contractions during the filling phase which may be spontaneous or provoked [5]. Detrusor overactivity is usually

associated with OAB syndrome characterised by urinary urgency, with or without urge urinary incontinence (UUI), usually with increased daytime frequency and nocturia, if there is no proven infection or other obvious pathology [18].

- Detrusor underactivity during voiding is characterised by decreased detrusor voiding pressure leading to a reduced urine flow rate. Detrusor underactivity causes OAB syndrome which is characterised by voiding symptoms similar to those caused by BPO [19].

Figure 1 illustrates the potential causes of LUTS. In any man complaining of LUTS, it is common for more than one of these factors to be present.

Figure 1: Causes of male LUTS



4. DIAGNOSTIC EVALUATION

Tests are useful for diagnosis, monitoring, assessing the risk of disease progression, treatment planning, and predicting treatment outcomes. The clinical assessment of patients with LUTS has two main objectives:

- to identify the differential diagnoses, since the origin of male LUTS is multifactorial, the relevant EAU Guidelines on the management of applicable conditions should be followed;
- to define the clinical profile (including the risk of disease progression) of men with LUTS in order to provide appropriate care.

4.1 Medical history

The importance of assessing the patient's history is well recognised [20-22]. A medical history aims to identify the potential causes and relevant co-morbidities, including medical and neurological diseases. In addition, current medication, lifestyle habits, emotional and psychological factors must be reviewed. The Panel recognises the need to discuss LUTS and the therapeutic pathway from the patient's perspective. This includes reassuring the patient that there is no definite link between LUTS and prostate cancer (PCa) [23, 24].

As part of the urological/surgical history, a self-completed validated symptom questionnaire (see section 4.2) should be obtained to objectify and quantify LUTS [20, 22]. Bladder diaries or frequency volume charts (FVC) are particularly beneficial (see section 4.3) [25]. Sexual function should also be assessed, preferably with validated symptom questionnaires such as the International Index of Erectile Function (IIEF) [26].

Summary of evidence	LE
A medical history is an integral part of a patient's medical evaluation.	4
A medical history aims to identify the potential causes of LUTS as well as any relevant co-morbidities and to review the patient's current medication and lifestyle habits.	4

Recommendation	Strength rating
Take a complete medical history from men with LUTS.	Strong

4.2 Symptom score questionnaires

All published guidelines for male LUTS recommend using validated symptom score questionnaires [20, 22]. Several questionnaires have been developed which are sensitive to symptom changes and can be used to monitor treatment [27-33]. Symptom scores are helpful in quantifying LUTS and in identifying which type of symptoms are predominant; however, they are not disease-, gender-, or age-specific. A systematic review (SR) evaluating the diagnostic accuracy of individual symptoms and questionnaires, compared with urodynamic studies (the reference standard), for the diagnosis of BOO in males with LUTS found that individual symptoms and questionnaires for diagnosing BOO were not significantly associated with one another [34].

4.2.1 The International Prostate Symptom Score (IPSS)

The IPSS is an eight-item questionnaire, consisting of seven symptom questions and one QoL question [28]. The IPSS score is categorised as 'asymptomatic' (0 points), 'mildly symptomatic' (1-7 points), 'moderately symptomatic' (8-19 points), and 'severely symptomatic' (20-35 points). Limitations include lack of assessment of incontinence, post-micturition symptoms, and bother caused by each separate symptom.

4.2.2 The International Consultation on Incontinence Questionnaire for Male LUTS (ICIQ-MLUTS)

The ICIQ-MLUTS was created from the International Continence Society (ICS) Male questionnaire. It is a widely used and validated patient completed questionnaire including incontinence questions and bother for each symptom [29]. It contains thirteen items, with subscales for nocturia and OAB, and is available in 24 languages. [35].

4.2.3 Danish Prostate Symptom Score (DAN-PSS)

The DAN-PSS [32] is a symptom score used mainly in Denmark and Finland. The DAN-PSS has twelve questions divided into parts A and B with questions on incontinence and measures the bother of each individual LUTS.

Summary of evidence	LE
Symptom questionnaires are sensitive to symptom changes.	3
Symptom scores can quantify LUTS and identify which types of symptoms are predominant; however, they are not disease-, gender-, or age-specific.	3

Recommendation	Strength rating
Use a validated symptom score questionnaire including bother and quality of life assessment during the initial assessment of male LUTS and for re-evaluation during and/or after treatment.	Strong

4.3 Frequency volume charts and/or bladder diaries

The recording of the volume and time of each void by the patient is referred to as an frequency volume chart (FVC). Inclusion of additional information such as fluid intake, use of pads, activities during recording, or which grades symptom severity and bladder sensation is termed a bladder diary [5]. Parameters that can be derived from the FVC and bladder diary include day-time and night-time voiding frequency, total voided volume, the fraction of urine production during the night (NP index), and volume of individual voids.

The mean 24-hour urine production is subject to considerable variation. Likewise, circumstantial influence and intra-individual variation cause FVC parameters to fluctuate, though there is comparatively little data [36, 37]. The FVC/bladder diary is particularly relevant in nocturia, where it underpins the categorisation of

underlying mechanism(s) [38-40]. The use of FVCs may cause a 'bladder training (BT) effect' and influence the frequency of nocturnal voids [41].

The duration of the FVC/bladder diary needs to be long enough to avoid sampling errors, but short enough to avoid non-compliance [25]. A SR of the available literature recommended FVCs should continue for at least three days [42]. There is no data as to whether the three days should be consecutive or scattered or whether it has to be on weekdays or weekends, as long as it is representative. The ICIQ-Bladder diary (ICIQ-BD) is the only diary that has undergone full validation [43].

Summary of evidence	LE
Frequency volume charts (FVC) and/or bladder diaries provide real-time documentation of urinary function and reduce recall bias.	3
Three day FVCs provide reliable measurement of urinary symptoms in patients with LUTS similar to seven days and without losing the diagnostic accuracy.	2b

Recommendations	Strength rating
Use a bladder diary to assess male LUTS with a storage component, especially nocturia.	Strong
Tell the patient to complete a bladder diary for at least three days.	Strong

4.4 Physical examination and digital-rectal examination

Physical examination particularly focusing on the suprapubic area, the external genitalia, the perineum, and lower limbs should be performed. Urethral discharge, meatal stenosis, phimosis, and penile cancer must be excluded.

4.4.1 Digital-rectal examination and prostate size evaluation

Digital-rectal examination (DRE) is the simplest way to assess prostate volume, but the correlation to prostate volume is poor. Quality-control procedures for DRE have been described [44]. Transrectal ultrasound (TRUS) is more accurate in determining prostate volume than DRE. There is an underestimation of prostate volume by DRE. The underestimation increases with increasing TRUS volume, particularly where the volume is > 30 mL [45]. A model of visual aids has been developed to help urologists estimate prostate volume more accurately [46]. One study concluded that DRE was sufficient to discriminate between prostate volumes > or < 50 mL [47].

Summary of evidence	LE
Physical examination is an integral part of a patient's medical evaluation.	4
Digital-rectal examination can be used to assess prostate volume and texture; however, the correlation to actual prostate volume is poor.	3

Recommendation	Strength rating
Perform a physical examination including digital rectal examination in the assessment of male LUTS.	Strong

4.5 Urinalysis

Urinalysis (dipstick or microscopy) must be included in the primary evaluation of any patient presenting with LUTS to identify conditions, such as urinary tract infections (UTI), microhaematuria and diabetes mellitus. If abnormal findings are detected further tests are recommended according to other EAU Guidelines, e.g., Guidelines on urinary tract cancers and urological infections [48-51].

Urinalysis is recommended in most Guidelines in the primary management of patients with LUTS [52, 53]. There is limited evidence, but general expert consensus suggests that the benefits outweigh the costs [54]. The value of urinary dipstick/microscopy for diagnosing UTI in men with LUTS without acute frequency and dysuria has been questioned [55].

Summary of evidence	LE
Urinalysis (dipstick or microscopy) may indicate a UTI, proteinuria, haematuria, or glycosuria requiring further assessment.	3
The benefits of urinalysis outweigh the costs.	4

Recommendation	Strength rating
Use urinalysis (by dipstick or microscopy) in the assessment of male LUTS.	Strong

4.6 Prostate-specific antigen

4.6.1 Prostate-specific antigen and the prediction of prostatic volume

Pooled analysis of randomised controll trials (RCTs), of men with LUTS and presumed BPO, showed that prostate-specific antigen (PSA) has a good predictive value for assessing prostate volume, with areas under the curve (AUC) of 0.76-0.78 for various prostate volume thresholds (30 mL, 40 mL, and 50 mL). To achieve a specificity of 70%, whilst maintaining a sensitivity between 65-70%, approximate age-specific criteria for detecting men with prostate glands exceeding 40 mL are PSA > 1.6 ng/mL, > 2.0 ng/mL, and > 2.3 ng/mL, for men with BPH in their 50s, 60s, and 70s, respectively [56].

A strong association between PSA and prostate volume was found in a large community-based study in the Netherlands [57]. A PSA threshold value of 1.5 ng/mL could best predict a prostate volume of > 30 mL, with a positive predictive value (PPV) of 78%. The prediction of prostate volume can also be based on total and free PSA. Both PSA forms predict the TRUS prostate volume (± 20%) in > 90% of the cases [58, 59].

4.6.2 Prostate-specific angtigen and the probability of PCa

The role of PSA in the diagnosis of PCa is presented by the EAU Guidelines on Prostate Cancer [60]. The potential benefits and harms of using serum PSA testing to diagnose PCa in men with LUTS should be discussed with the patient.

4.6.3 Prostate-specific antigen and the prediction of BPO-related outcomes

Serum PSA is a stronger predictor of prostate growth than prostate volume [61]. In addition, an RCT showed that PSA also predicted the changes in symptoms, QoL/bother, and maximum flowrate (Q_{max}) [62]. In a longitudinal study of men managed conservatively, PSA was a highly significant predictor of clinical progression to urinary retention [63, 64]. In the placebo arms of large double-blind studies, baseline serum PSA predicted the risk of acute urinary retention (AUR) and BPO-related surgery [65, 66]. An equivalent link was also confirmed by the Olmsted County Study. The risk for treatment was higher in men with a baseline PSA of > 1.4 ng/mL [67]. Patients with BPO seem to have a higher PSA level and larger prostate volumes. The PPV of PSA for the detection of BPO was recently shown to be 68% [68]. Furthermore, in an epidemiological study, elevated free PSA levels could predict clinical BPE, independent of total PSA levels [69].

Summary of evidence	LE
Prostate-specific antigen has a good predictive value for assessing prostate volume and is a strong predictor of prostate growth.	1b
Baseline PSA can predict the risk of AUR and BPO related surgery.	1b

Recommendations	Strength rating
Measure prostate-specific antigen (PSA) if a diagnosis of prostate cancer will change management.	Strong
Measure PSA if it assists in the treatment and/or decision-making process.	Strong
Counsel patients about PSA testing and the implications of a raised PSA test.	Strong

4.7 Renal function measurement

Renal function may be assessed by serum creatinine or estimated glomerular filtration rate (eGFR). Hydronephrosis, renal insufficiency or urinary retention are more prevalent in patients with signs or symptoms of BPO [70]. Even though BPO may be responsible for these complications, there is no conclusive evidence on the mechanism [71].

One study reported that 11% of men with LUTS had renal insufficiency [70]. Neither symptom score nor QoL was associated with the serum creatinine level. Diabetes mellitus or hypertension were the most likely causes of the elevated creatinine concentration. Comiter *et al*., [72] reported that non-neurogenic voiding dysfunction is not a risk factor for elevated creatinine levels. Koch *et al*., [73] concluded that only those with an elevated creatinine level or reduced eGFR require investigational ultrasound (US) of the kidney and bladder to assess post-void residual.

In the Olmsted County Study, there was a cross-sectional association between signs and symptoms of BPO (though not prostate volume) and chronic kidney disease (CKD) [74]. In 2,741 consecutive patients who presented with LUTS, decreased Q_{max}, a history of hypertension and/or diabetes were associated with CKD [75]. Another study demonstrated a correlation between Q_{max} and eGFR in middle-aged men with moderate-to-severe LUTS [76]. Patients with renal insufficiency are at an increased risk of developing post-operative complications [77].

Summary of evidence	LE
Decreased Q_{max} and a history of hypertension and/or diabetes are associated with CKD in patients who present with LUTS.	3
Patients with renal insufficiency are at an increased risk of developing post-operative complications.	3

Recommendation	Strength rating
Assess renal function if renal impairment is suspected based on history and clinical examination, or in the presence of hydronephrosis, or when considering surgical treatment for male LUTS.	Strong

4.8 Post-void residual urine

Post-void residual (PVR) urine can be assessed by transabdominal ultrasound (US), bladder scan or catheterisation. Post-void residual is not necessarily associated with BOO, since high PVR volumes can be a consequence of obstruction and/or poor detrusor function/DU [78, 79]. Using a PVR threshold of 50 mL, the diagnostic accuracy of PVR measurement has a PPV of 63% and a negative predictive value (NPV) of 52% for the prediction of BOO [80]. A large PVR is not a contraindication to watchful waiting (WW) or medical therapy, although it may indicate a poor response to treatment and especially to WW. In both the MTOPS and ALTESS studies, a high baseline PVR was associated with an increased risk of symptom progression [65, 66].

Monitoring of changes in PVR over time may allow for identification of patients at risk of AUR [81]. This is of importance for the treatment of patients using antimuscarinic medication. In contrast, baseline PVR has little prognostic value for the risk of BPO-related invasive therapy in patients on α1-blockers or WW [82]. However, due to large test-retest variability and lack of outcome studies, no PVR threshold for treatment decision has yet been established; this is a research priority.

Summary of evidence	LE
The diagnostic accuracy of PVR measurement, using a PVR threshold of 50 mL, has a PPV of 63% and a NPV of 52% for the prediction of BOO.	3
Monitoring of changes in PVR over time may allow for identification of patients at risk of AUR.	3

Recommendation	Strength rating
Measure post-void residual in the assessment of male LUTS.	Weak

4.9 Uroflowmetry

Urinary flow rate assessment is a widely used non-invasive urodynamic test. Key parameters are Q_{max}, voided volume, PVR, and flow pattern. Uroflowmetry parameters should preferably be evaluated with voided volume >150mL. As Q_{max} is prone to within-subject variation [83, 84], it is useful to repeat uroflowmetry measurements, especially if the voided volume is < 150 mL, or Q_{max} or flow pattern is abnormal.

The diagnostic accuracy of uroflowmetry for detecting BOO varies considerably and is substantially influenced by threshold values. A threshold Q_{max} of 10 mL/s has a specificity of 70%, a PPV of 70% and a sensitivity of 47% for BOO. The specificity using a threshold Q_{max} of 15 mL/s was 38%, the PPV 67% and the sensitivity 82% [85]. If Q_{max} is > 15 mL/s, physiological compensatory processes mean that BOO cannot be excluded. Low Q_{max} can arise as a consequence of BOO [86], DU or an under-filled bladder [87]. Therefore, it is limited as a diagnostic test as it is unable to discriminate between the underlying mechanisms. Specificity can be improved by repeated flow rate testing.

Uroflowmetry can be used for monitoring treatment outcomes [88] and correlating symptoms with objective findings [85, 89].

Summary of evidence	LE
The diagnostic accuracy of uroflowmetry for detecting BOO varies considerably and is substantially influenced by threshold values. Specificity can be improved by repeated flow rate testing.	2b

Recommendations	Strength rating
Perform uroflowmetry in the initial assessment of male LUTS.	Weak
Perform uroflowmetry prior to medical or invasive treatment.	Strong

4.10 Imaging

*4.10.1 **Upper urinary tract***

Men with LUTS are not at increased risk for upper tract malignancy or other abnormalities when compared to the overall population [73, 90-92]. Several arguments support the use of renal US in preference to intravenous urography. Ultrasound allows for better characterisation of renal masses, the possibility of investigating the liver and retroperitoneum, and simultaneous evaluation of the bladder, PVR and prostate, together with a lower cost, no radiation dose and less side effects [90]. Ultrasound can be used for the evaluation of men with large PVR, haematuria, or a history of urolithiasis.

Summary of evidence	LE
Men with LUTS are not at increased risk for upper tract malignancy or other abnormalities when compared to the overall population.	3
Ultrasound can be used for the evaluation of men with large PVR, haematuria, or a history of urolithiasis.	4

Recommendation	Strength rating
Perform ultrasound of the upper urinary tract in men with LUTS.	Weak

*4.10.2 **Prostate***

Imaging of the prostate can be performed by transabdominal US, TRUS, computed tomography (CT), and magnetic resonance imaging (MRI). However, in daily practice, prostate imaging is performed by transabdominal (suprapubic) US or TRUS [90].

4.10.2.1 Prostate size and shape

Assessment of prostate size is important for the selection of interventional treatment, i.e., open prostatectomy (OP), enucleation techniques, transurethral resection, transurethral incision of the prostate (TUIP), or minimally invasive therapies. It is also important prior to treatment with 5α-reductase inhibitors (5-ARIs). Prostate volume predicts symptom progression and the risk of complications [92].

Transrectal US is superior to transabdominal volume measurement [93, 94]. The presence of a median lobe may guide treatment choice in patients scheduled for a minimally invasive approach since medial lobe presence can be a contraindication for some minimally invasive treatments (see section 5.3).

Summary of evidence	LE
Assessment of prostate size by TRUS or transabdominal US is important for the selection of interventional treatment and prior to treatment with 5-ARIs.	3

Recommendations	Strength rating
Perform imaging of the prostate when considering medical treatment for male LUTS, if it assists in the choice of the appropriate drug.	Weak
Perform imaging of the prostate when considering surgical treatment.	Strong

*4.10.3 **Voiding cysto-urethrogram***

Voiding cysto-urethrogram (VCUG), on its own, is not recommended in the routine diagnostic work-up of men with LUTS, but it may be useful for the detection of vesico-ureteral reflux, bladder diverticula, or urethral diseases and can be combined with urodynamics in the form of video-urodynamics. Retrograde urethrography may additionally be useful for the evaluation of suspected urethral strictures.

4.11 Urethrocystoscopy

Patients with a history of microscopic or gross haematuria, urethral stricture, or bladder cancer, who present with LUTS, should undergo urethrocystoscopy during diagnostic evaluation. The evaluation of a prostatic middle lobe with urethrocystoscopy should be performed when considering interventional treatments for which the presence of middle lobe may affect the treatment offered e.g., Urolift.

A prospective study evaluated 122 patients with LUTS using uroflowmetry and urethrocystoscopy [95]. The pre-operative Q_{max} was normal in 25% of 60 patients who had no bladder trabeculation, 21% of 73 patients with mild trabeculation and 12% of 40 patients with marked trabeculation on cystoscopy. All 21 patients who presented with diverticula had a reduced Q_{max}.

Another study showed that there was no significant correlation between the degree of bladder trabeculation (graded from I to IV), and the pre-operative Q_{max} value in 39 symptomatic men aged 53-83 years [96]. The largest study published on this issue examined the relation of urethroscopic findings to urodynamic

studies in 492 elderly men with LUTS [97]. The authors noted a correlation between cystoscopic appearance (grade of bladder trabeculation and urethral occlusion) and urodynamic indices, DO and low compliance. It should be noted, however, that BOO was present in 15% of patients with normal cystoscopic findings, while 8% of patients had no obstruction, even in the presence of severe trabeculation [97].

Summary of evidence	LE
Patients with a history of microscopic or gross haematuria, urethral stricture, or bladder cancer, who present with LUTS, should undergo urethrocystoscopy during diagnostic evaluation.	3
No study clearly identified a strong association between the urethrocystoscopic and urodynamic findings.	3

Recommendation	Strength rating
Perform urethrocystoscopy in men with LUTS prior to minimally invasive/surgical therapies if the findings may change treatment.	Weak

4.12 Urodynamics

In male LUTS, the most widespread invasive urodynamic techniques employed are filling cystometry and pressure flow studies (PFS). The major goal of urodynamics (UDS) is to explore the functional mechanisms of LUTS, to identify risk factors for adverse outcomes and to provide information for shared decision-making. Most terms and conditions (e.g., DO, low compliance, BOO/BPO, DU) are defined by urodynamic investigation.

4.12.1 Diagnosing bladder outlet obstruction

Pressure flow studies are used to diagnose and define the severity of BOO, which is characterised by increased detrusor pressure and decreased urinary flow rate during voiding. Bladder outlet obstruction/BPO has to be differentiated from DU, which exhibits decreased detrusor pressure during voiding in combination with decreased urinary flow rate [5].

Urodynamic testing may also identify DO. Studies have described an association between BOO and DO [98, 99]. In men with LUTS attributed to BPO, DO was present in 61% and independently associated with BOO grade and ageing [98].

The prevalence of DU in men with LUTS is 11-40% [100, 101]. Detrusor contractility does not appear to decline in long-term BOO and surgical relief of BOO does not improve contractility [102, 103]. The UPSTREAM trial investigated whether urodynamics would reduce surgery without increasing urinary symptoms. UPSTREAM was a non-inferiority, RCT in men with bothersome LUTS, in whom surgery was an option, in 26 hospitals in England. In the UDS arm, 153/408 patients (38%) received surgery compared with 138/384 (36%) in the routine care (RC) arm. A total of 428 adverse events were recorded, with related events similar in both arms and eleven unrelated deaths. The UDS group was non-inferior to the RC group for IPSS, and UDS did not significantly reduce surgical rates. The authors concluded that routine use of UDS in the evaluation of uncomplicated LUTS has a limited role and should be used selectively [104]. If urodynamic investigation is performed, a rigorous quality control is mandatory [105, 106].

Due to the invasive nature of the test, a urodynamic investigation is generally only offered if conservative and medical treatment have failed. The Guidelines Panel attempted to identify specific indications for UDS based on age, findings from other diagnostic tests and previous treatments. The Panel allocated a different degree of obligation for UDS in men > 80 years and men < 50 years, which reflects the lack of evidence. In addition, there was no consensus whether UDS should or may be performed when considering surgery in men with bothersome predominantly voiding LUTS and Q_{max} > 10 mL/s, although the Panel recognised that with a Q_{max} < 10 mL/s, BOO is likely and UDS is not necessarily needed.

Patients with neurological disease, including those with previous radical pelvic surgery, should be assessed according to the EAU Guidelines on Neuro-Urology [107].

4.12.2 Videourodynamics

Videourodynamics provides additional anatomical and functional information and may be recommended if the clinician considers this is needed to understand the pathophysiological mechanism of an individual patient's LUTS.

Summary of evidence	LE
Pressure-flow studies is not a test for routine use prior to prostate surgery for all patients	3

Recommendations	Strength rating
Perform pressure-flow studies (PFS) only in individual patients for specific indications prior to invasive treatment or when further evaluation of the underlying pathophysiology of LUTS is warranted.	Weak
Perform PFS in men who have had previous unsuccessful (invasive) treatment for LUTS.	Weak
Perform PFS in men considering invasive treatment who cannot void > 150 mL.	Weak
Perform PFS when considering surgery in men with bothersome predominantly voiding LUTS and Q_{max} > 10 mL/s.	Weak
Perform PFS when considering invasive therapy in men with bothersome, predominantly voiding LUTS with a post void residual > 300 mL.	Weak
Perform PFS when considering invasive treatment in men with bothersome, predominantly voiding LUTS aged > 80 years.	Weak
Perform PFS when considering invasive treatment in men with bothersome, predominantly voiding LUTS aged < 50 years.	Weak

4.13 Non-invasive tests in diagnosing bladder outlet obstruction in men with LUTS

4.13.1 Prostatic configuration/intravesical prostatic protrusion

Prostatic configuration can be evaluated with TRUS, using the concept of the presumed circle area ratio (PCAR) [108]. The PCAR evaluates how closely the transverse US image of the prostate approaches a circular shape. The ratio tends toward one as the prostate becomes more circular. The sensitivity of PCAR was 77% for diagnosing BPO when PCAR was > 0.8, with 75% specificity [108].

Ultrasound measurement of intravesical prostatic protrusion (IPP) assesses the distance between the tip of the prostate median lobe and bladder neck in the midsagittal plane, using a suprapubically positioned US scanner, with a bladder volume of 150-250 mL; grade I protrusion is 0-4.9 mm, grade II is 5-10 mm and grade III is > 10 mm.

Intravesical prostatic protrusion correlates well with BPO (presence and severity) on urodynamic testing, with a PPV of 94% and a NPV of 79% [109]. Intravesical prostatic protrusion may also correlate with prostate volume, DO, bladder compliance, detrusor pressure at maximum urinary flow, BOO index and PVR, and negatively correlates with Q_{max} [110]. Furthermore, IPP also appears to successfully predict the outcome of a trial without catheter after AUR [111, 112]. However, no information with regards to intra- or inter-observer variability and learning curve is yet available. Therefore, whilst IPP may be a feasible option to infer BPO in men with LUTS, the role of IPP as a non-invasive alternative to PFS in the assessment of male LUTS remains under evaluation.

4.13.2 Bladder/detrusor wall thickness and ultrasound-estimated bladder weight

For bladder wall thickness (BWT) assessment, the distance between the mucosa and the adventitia is measured. For detrusor wall thickness (DWT) assessment, the only measurement needed is the detrusor sandwiched between the mucosa and adventitia [113].

A correlation between BWT and UDS parameters has been reported. A threshold value of 5 mm at the anterior bladder wall with a bladder filling of 150 mL was best at differentiating between patients with or without BOO [114]. Detrusor wall thickness at the anterior bladder wall with a bladder filling > 250 mL (threshold value for BOO > 2 mm) has a PPV of 94% and a specificity of 95%, achieving 89% agreement with PFS [73]. Threshold values of 2.0, 2.5, or 2.9 mm for DWT in patients with LUTS are able to identify 81%, 89%, and 100% of patients with BOO, respectively [115].

All studies found that BWT or DWT measurements have a higher diagnostic accuracy for detecting BOO than Q_{max} or Q_{ave} of free uroflowmetry, measurements of PVR, prostate volume, or symptom severity. One study could not demonstrate any difference in BWT between patients with normal UDS, BOO or DO. However, the study did not use a specific bladder filling volume for measuring BWT [116]. Disadvantages of the method include the lack of standardisation, and lack of evidence to indicate which measurement (BWT/DWT) is preferable [117]. Measurement of BWT/DWT is therefore not recommended for the diagnostic work-up of men with LUTS.

Ultrasound-estimated bladder weight (UEBW) may identify BOO with a diagnostic accuracy of 86% at a cut-off value of 35 g [118, 119]. Severe LUTS and a high UEBW (> 35 g) are risk factors for prostate/BPO surgery in men on α-blockers [120].

4.13.3 Non-invasive pressure-flow testing

The penile cuff method, in which flow is interrupted to estimate isovolumetric bladder pressure, shows promising data, with good test repeatability [121] and interobserver agreement [122]. A nomogram has also been derived [123] whilst a method in which flow is not interrupted is also under investigation [124].

The data generated with the external condom method [125] correlates with invasive PFS in a high proportion of patients [126]. Resistive index [127] and prostatic urethral angle [128] have also been proposed, but are still experimental.

4.13.4 The diagnostic performance of non-invasive tests in diagnosing bladder outlet obstruction in men with LUTS compared with pressure-flow studies

A SR including 42 studies investigated the diagnostic performance of non-invasive tests in diagnosing BOO in men with LUTS compared with UDS/PFS [129]. The majority of the included studies were prospective cohorts, and the diagnostic accuracy of the following non-invasive tests were assessed: penile cuff test; uroflowmetry; DWT/BWT; bladder weight; external condom catheter method; IPP; Doppler US; prostate volume/height; and near-infrared spectroscopy. Overall, although the majority of studies have a low risk of bias, data regarding the diagnostic accuracy of these non-invasive tests is limited by the heterogeneity of the studies in terms of the threshold values used to define BOO, the different urodynamic definitions of BOO used across different studies and the small number of studies for each test. It was found that specificity, sensitivity, PPV and NPV of the non-invasive tests were highly variable. Therefore, even though several tests have shown promising results regarding non-invasive diagnosis of BOO, invasive urodynamics remains the modality of choice.

Summary of evidence	LE
Data regarding the diagnostic accuracy of non-invasive tests is limited by the heterogeneity of the studies as well as the small number of studies for each test.	1a
Specificity, sensitivity, PPV and NPV of the non-invasive tests were highly variable.	1a

Recommendation	Strength rating
Do not offer non-invasive tests as an alternative to urodynamics/pressure-flow studies for diagnosing bladder outflow obstruction in men.	Strong

4.14 Novel assessment

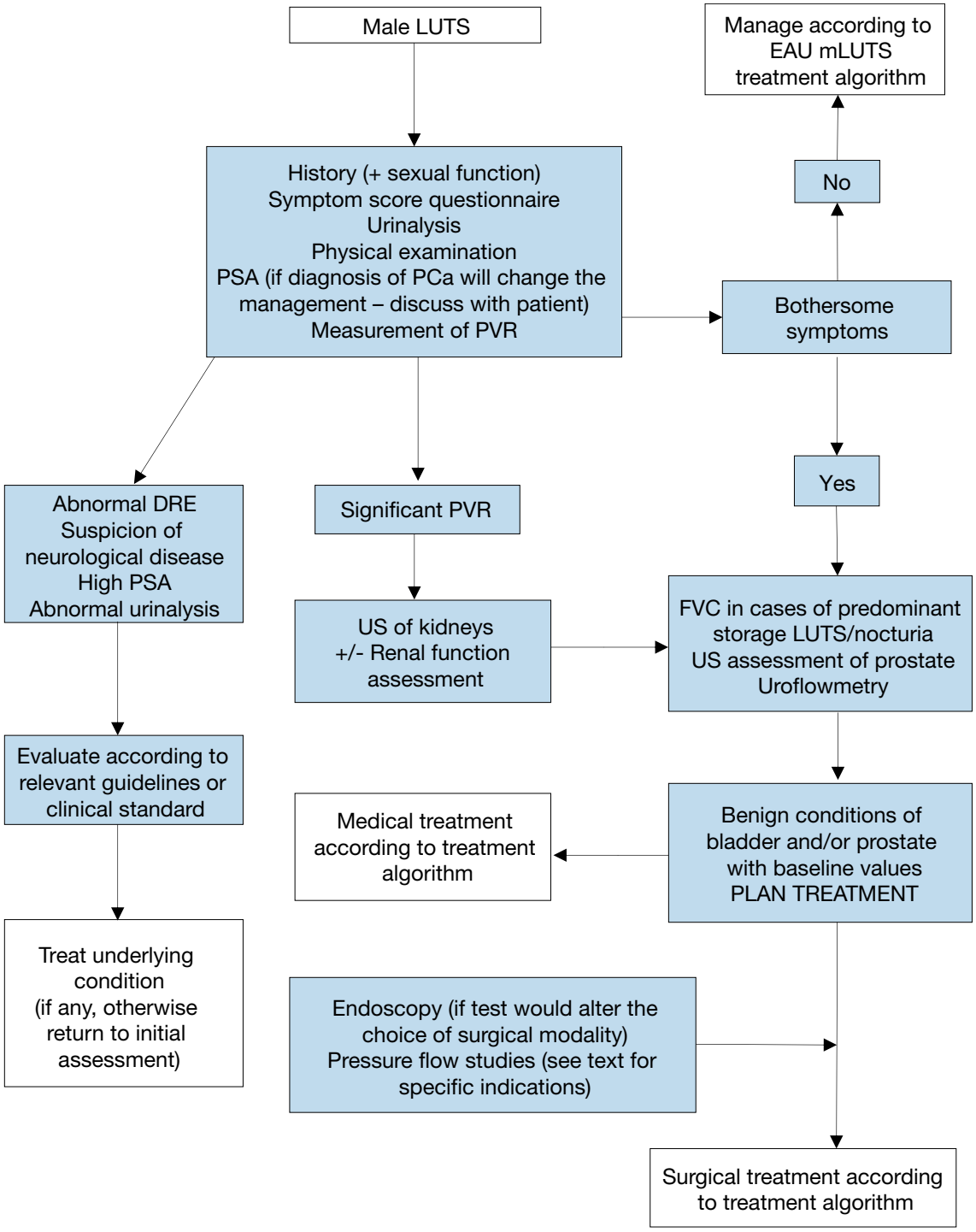
4.14.1 Visual prostate symptom score

A novel visual prostate symptom score (VPSS) has been prospectively tested vs. the IPPS and correlated positively with the IPSS score [130, 131]. This visual score can be used as an option in men with limited literacy.

4.14.2 Micro-RNA

The use of miR-221 has been shown to have the potential to be used as a biomarker and novel target in the early diagnosis and therapy of BPH [132].

Figure 2: Assessment algorithm of LUTS in men aged 40 years or older
Readers are strongly recommended to read the full text that highlights the current position of each test in detail.



DRE = digital-rectal examination; FVC = frequency volume chart; LUTS = lower urinary tract symptoms; PCa = prostate cancer; PSA = prostate specific antigen; PVR = post-void residual; US = ultrasound.

5. DISEASE MANAGEMENT

5.1 Conservative treatment

5.1.1 Watchful waiting

Many men with LUTS are not troubled enough by their symptoms to need drug treatment or surgical intervention. All men with LUTS should be formally assessed prior to any allocation of treatment in order to establish symptom severity and to differentiate between men with uncomplicated (the majority) and complicated LUTS. Watchful waiting is a viable option for many men with non-bothersome LUTS as few will progress to AUR and complications (e.g. renal insufficiency or stones) [133, 134], whilst others can remain stable for years [135]. In one study, approximately 85% of men with mild LUTS were stable on WW at one year [136].

A study comparing WW and transurethral resection of the prostate (TURP) in men with moderate LUTS showed the surgical group had improved bladder function (flow rates and PVR volumes), especially in those with high levels of bother; 36% of WW patients crossed over to surgery within five years, leaving 64% doing well in the WW group [137, 138]. Increasing symptom bother and PVR volumes are the strongest predictors of WW failure. Men with mild-to-moderate uncomplicated LUTS who are not too troubled by their symptoms are suitable for WW.

5.1.2 Behavioural and dietary modifications

It is customary for this type of management to include the following components:

- education (about the patient's condition);
- reassurance (that cancer is not a cause of the urinary symptoms);
- periodic monitoring;
- lifestyle advice [135, 136, 139, 140] such as:
    - reduction of fluid intake at specific times aimed at reducing urinary frequency when most inconvenient (e.g., at night or when going out in public);
    - avoidance/moderation of intake of caffeine or alcohol, which may have a diuretic and irritant effect, thereby increasing fluid output and enhancing frequency, urgency and nocturia;
    - use of relaxed and double-voiding techniques;
    - urethral milking to prevent post-micturition dribble;
    - distraction techniques such as penile squeeze, breathing exercises, perineal pressure, and mental tricks to take the mind off the bladder and toilet, to help control OAB symptoms;
    - bladder retraining that encourages men to hold on when they have urgency to increase their bladder capacity and the time between voids;
    - reviewing the medication and optimising the time of administration or substituting drugs for others that have fewer urinary effects (these recommendations apply especially to diuretics);
    - providing necessary assistance when there is impairment of dexterity, mobility, or mental state;
    - treatment of constipation.

Evidence exists that self-management as part of WW reduces both symptoms and progression [139, 140]. Men randomised to three self-care management sessions in addition to standard care had better symptom improvement and QoL than men treated with standard care only, for up to a year [139]. A SR and meta-analysis found reasonable certainty in estimates that self-management intervention significantly reduced symptom severity in terms of IPSS at six months compared with usual care [141]. The reduction in IPSS score with self-management was similar to that achieved with drug therapy at six to twelve weeks. Self-management had a smaller, additional benefit at six weeks when added to drug therapy [141].

5.1.3 Practical considerations

The components of self-care management have not been individually studied. The above components of lifestyle advice have been derived from formal consensus methodology [142]. Further research in this area is required.

Summary of evidence	LE
Watchful waiting is usually a safe alternative for men who are less bothered by urinary difficulty or who wish to delay treatment. The treatment failure rate over a period of five years was 21%; 79% of patients were clinically stable.	1b
An additional study reported 81% of patients were clinically stable on WW after a mean follow-up of seventeen months.	2

Men randomised to three self-management sessions in addition to standard care had better symptom improvement and QoL than men treated with standard care alone at up to a year. Self-care management as part of WW reduces both symptoms and progression.	1b
Self-management achieved a clinically meaningful reduction in symptom severity at six months compared to usual care. There was also a small but significant additional benefit of adding self-management to drug therapy.	1b

Recommendations	Strength rating
Offer men with mild/moderate symptoms, minimally bothered by their symptoms, watchful waiting.	Strong
Offer men with LUTS lifestyle advice and self-care information prior to, or concurrent with, treatment.	Strong

5.2 Pharmacological treatment

5.2.1 Alpha 1-Adrenoceptor antagonists (α1-blockers)

Mechanism of action: Alpha 1-blockers aim to inhibit the effect of endogenously released noradrenaline on smooth muscle cells in the prostate and thereby reduce prostate tone and BOO [143]. However, α1-blockers have little effect on urodynamically determined bladder outlet resistance [144], and treatment-associated improvement of LUTS correlates poorly with obstruction [145]. Thus, other mechanisms of action may also be relevant.

Alpha 1-adrenoceptors located outside the prostate (e.g. urinary bladder and/or spinal cord) and α1-adrenoceptor subtypes (α1B- or α1D-adrenoceptors) may play a role as mediators of effects. Alpha 1-adrenoceptors in blood vessels, other non-prostatic smooth muscle cells, and the central nervous system may mediate adverse events.

Currently available α1-blockers are: alfuzosin hydrochloride (alfuzosin); doxazosin mesylate (doxazosin); silodosin; tamsulosin hydrochloride (tamsulosin); terazosin hydrochloride (terazosin); and naftopidil. Alpha 1-blockers exist in different formulations. Although different formulations result in different pharmacokinetic and tolerability profiles, the overall difference in clinical efficacy between the difference formulations seems negligible.

Efficacy: Indirect comparisons and limited direct comparisons between α1-blockers demonstrate that all α1-blockers have a similar efficacy in appropriate doses [146]. Clinical effects take a few weeks to develop fully, but significant efficacy over placebo can occur within hours to days [145].

Controlled studies show that α1-blockers typically reduce IPSS by approximately 30-40% and increase Q_{max} by approximately 20-25%. However, substantial improvements also occurred in the corresponding placebo arms [63, 147]. In open-label studies, an IPSS improvement of up to 50% and Q_{max} increase of up to 40% were documented [63, 147]. A recent SR and meta-analysis suggested that Q_{max} variation underestimates the real effect of α1-blockers on BPO, as small improvements in Q_{max} correspond to relevant improvements in BOO index in PFS [148].

Alpha 1-blockers can reduce both storage and voiding LUTS. Prostate size does not affect α1-blocker efficacy in studies with follow-up periods of less than one year, but α1-blockers do seem to be more efficacious in patients with smaller prostates (< 40 mL) in longer-term studies [65, 149-152]. The efficacy of α1-blockers is similar across age groups [147]. A pooled analysis of phase III and IV trials of silodosin 8 mg demonstrated that improvements in total, storage, voiding, and QoL IPSS scores were similar for the severe and not severe LUTS cohorts [153]. In addition, α1-blockers neither reduce prostate size nor prevent AUR in long-term studies [150-152]; however, recent evidence suggests that the use of α1-blockers (alfuzosin and tamsulosin) may improve resolution of AUR [154]. Nonetheless, IPSS reduction and Q_{max} improvement during α1-blocker treatment appears to be maintained over at least four years.

Tolerability and safety: Tissue distribution, subtype selectivity, and pharmacokinetic profiles of certain formulations may contribute to the tolerability profile of specific drugs. The most frequent adverse events of α1-blockers are asthenia, dizziness and (orthostatic) hypotension. Vasodilating effects are most pronounced with doxazosin and terazosin and are less common with alfuzosin and tamsulosin [155]. Patients with cardiovascular co-morbidity and/or vaso-active co-medication may be susceptible to α1-blocker-induced vasodilatation [156]. In contrast, the frequency of hypotension with the α1A-selective blocker silodosin is comparable with placebo [157]. In a large retrospective cohort analysis of men aged > 66 years treated with α1-blockers the risks of falling (odds ratio [OR] 1.14) and of sustaining a fracture (OR 1.16) was increased, most likely as a result of induced hypotension [158].

An adverse ocular event termed intra-operative floppy iris syndrome (IFIS) was reported in 2005, affecting cataract surgery [159]. A meta-analysis on IFIS after alfuzosin, doxazosin, tamsulosin or terazosin exposure showed an increased risk for all α1-blockers [160]. However, the OR for IFIS was much higher for

tamsulosin. It appears prudent not to initiate α1-blocker treatment prior to scheduled cataract surgery, and the ophthalmologist should be informed about α1-blocker use.

A SR concluded that α1-blockers do not adversely affect libido, have a small beneficial effect on erectile function (ED), but can cause abnormal ejaculation [161]. Originally, abnormal ejaculation was thought to be retrograde, but more recent data demonstrate that it is due to a decrease or absence of seminal fluid during ejaculation, with young age being an apparent risk factor. In a recent meta-analysis ejaculatory dysfunction (EjD) was significantly more common with α1-blockers than with placebo (OR: 5.88). In particular, EjD was significantly more commonly related with tamsulosin or silodosin (OR: 8.57 and 32.5) than placebo, while both doxazosin and terazosin (OR: 0.80 and 1.78) were associated with a low risk of EjD [162]. In the meta-regression, the occurrence of EjD was independently associated with the improvement of urinary symptoms and flow rate, suggesting that the more effective the α1-blocker is the greater the incidence of EjD.

Practical considerations: Alpha 1-blockers are usually considered the first-line drug treatment for male LUTS because of their rapid onset of action, good efficacy, and low rate and severity of adverse events. However, α1-blockers do not prevent occurrence of urinary retention or need for surgery. Ophthalmologists should be informed about α1-blocker use prior to cataract surgery. Elderly patients treated with non-selective α1-blockers should be informed about the risk of orthostatic hypotension. Sexually active patients treated with selective α1-blockers should be counselled about the risk of EjD.

Summary of evidence	LE
Alpha 1-blockers are effective in reducing urinary symptoms (IPSS) and increasing the peak urinary flow rate (Q_{max}) compared with placebo.	1a
Alfuzosin, terazosin and doxazosin showed a statistically significant increased risk of developing vascular-related events compared with placebo.	1a
Alfuzosin, doxazosin, tamsulosin or terazosin exposure has been associated with an increased risk of IFIS.	1a
Ejaculatory dysfunction is significantly more common with α1-blockers than with placebo, particularly with more selective α1-blockers such as tamsulosin and silodosin.	1a

Recommendation	Strength rating
Offer α1-blockers to men with moderate-to-severe LUTS.	Strong

5.2.2 5α-reductase inhibitors

Mechanism of action: Androgen effects on the prostate are mediated by dihydrotestosterone (DHT), which is converted from testosterone by the enzyme 5α-reductase [163], which has two isoforms:

- 5α-reductase type 1: predominant expression and activity in the skin and liver.
- 5α-reductase type 2: predominant expression and activity in the prostate.

Two 5-ARIs are available for clinical use: dutasteride and finasteride. Finasteride inhibits only 5α-reductase type 2, whereas dutasteride inhibits both 5α-reductase types (dual 5-ARI). The 5-ARIs induce apoptosis of prostate epithelial cells [164] leading to prostate size reduction of about 18-28% and a decrease in circulating PSA levels of about 50% after six to twelve months of treatment [165]. Mean prostate volume and PSA reduction may be even more pronounced after long-term treatment. Continuous treatment reduces the serum DHT concentration by approximately 70% with finasteride and 95% with dutasteride. However, prostate DHT concentration is reduced to a similar level (85-90%) by both 5-ARIs.

Efficacy: Clinical effects relative to placebo are seen after treatment of at least six months. After two to four years of treatment 5-ARIs improve IPSS by approximately 15-30%, decrease prostate volume by 18-28%, and increase Q_{max} by 1.5-2.0 mL/s in patients with LUTS due to prostate enlargement [65, 151, 152, 166-172]. An indirect comparison and one direct comparative trial (twelve months duration) indicated that dutasteride and finasteride are equally effective in the treatment of LUTS [165, 173]. Symptom reduction depends on initial prostate size.

Finasteride may not be more efficacious than placebo in patients with prostates < 40 mL [174]. However, dutasteride seems to reduce IPSS, prostate volume, and the risk of AUR, and to increase Q_{max} even in patients with prostate volumes of between 30 and 40 mL [175, 176]. A long-term trial with dutasteride in symptomatic men with prostate volumes > 30 mL and increased risk for disease progression showed that dutasteride reduced LUTS at least as much as the α1-blocker tamsulosin [151, 172, 177]. The greater the baseline prostate volume (or serum PSA level), the faster and more pronounced the symptomatic benefit of dutasteride as compared to tamsulosin.

5α-reductase inhibitors, but not α1-blockers, reduce the long-term (> 1 year) risk of AUR or need for surgery [65, 170, 178]. In the PLESS study, finasteride reduced the relative risk of AUR by 57% and need for surgery by 55% (absolute risk reduction 4% and 7%, respectively) at four years, compared with placebo [170]. In the MTOPS study, finasteride reduced the relative risk of AUR by 68% and need for surgery by 64% (absolute risk reduction 2% and 3%, respectively), also at four years [65]. A pooled analysis of three RCTs with two-year follow-up data, reported that treatment with finasteride decreased the relative risk of AUR by 57%, and surgical intervention by 34% (absolute risk reduction 2% for both) in patients with moderately symptomatic LUTS [179]. Dutasteride has also demonstrated efficacy in reducing the risks for AUR and BPO-related surgery. Open-label trials have demonstrated relevant changes in urodynamic parameters [180, 181]. Furthermore, finasteride might reduce blood loss during transurethral prostate surgery, probably due to its effects on prostatic vascularisation [182, 183].

Tolerability and safety: The most common adverse events are reduced libido, erectile dysfunction (ED) and less frequently, ejaculation disorders such as retrograde ejaculation, ejaculation failure, or decreased semen volume [65, 152, 165, 184]. Gynaecomastia (with breast or nipple tenderness) develops in 1-2% of patients. Two studies have suggested that treatment with 5-ARIs is associated with a higher incidence of high-grade cancers although no causal relationship has been proven [185, 186]. There is a long-standing debate regarding potential cardiovascular side effects of 5-ARIs, in particular dutasteride [187]. Population-based studies in Taiwan and Ontario did not find an association between the use of 5-ARIs and increased cardiovascular side effects [187, 188]. In a British-Taiwanese population-based cohort study, the risk of type II diabetes was higher in men with 5-ARIs than in men receiving tamsulosin but did not differ between dutasteride and finasteride [189].

Practical considerations: Treatment with 5-ARIs should be considered in men with moderate-to-severe LUTS and an enlarged prostate (> 40 mL) and/or elevated PSA concentration (> 1.4-1.6 ng/mL). They can prevent the risk of AUR and need for surgery. Due to the slow onset of action, they are not suitable for short-term use. Their effect on PSA needs to be considered in relation to PCa screening.

Summary of evidence	**LE**
After two to four years of treatment, 5-ARIs improve IPSS by approximately 15-30%, de-crease prostate volume by 18-28%, and increase Q_{max} by 1.5-2.0 mL/s in patients with LUTS due to prostate enlargement.	1b
5α-reductase inhibitors can prevent disease progression with regard to AUR and the need for surgery. Due to 5-ARIs slow onset of action, they are suitable only for long-term treatment (years).	1a
The most relevant adverse effects of 5-ARIs are related to sexual function, and include reduced libido, ED and less frequently, ejaculation disorders such as retrograde ejaculation, ejaculation failure, or decreased semen volume.	1b

Recommendations	**Strength rating**
Use 5α-reductase inhibitors (5-ARIs) in men who have moderate-to-severe LUTS and an increased risk of disease progression (e.g., prostate volume > 40 mL).	Strong
Counsel patients about the slow onset of action of 5-ARIs.	Strong

*5.2.3 **Muscarinic receptor antagonists***

Mechanism of action: The detrusor is innervated by parasympathetic nerves whose main neurotransmitter is acetylcholine, which stimulates muscarinic receptors (M-cholinoreceptors) on the smooth muscle cells. Muscarinic receptors are also present on other cell types, such as bladder urothelial cells and epithelial cells of the salivary glands. Five muscarinic receptor subtypes (M1-M5) have been described, of which M2 and M3 are predominant in the detrusor. The M2 subtype is more numerous, but the M3 subtype is functionally more important in bladder contractions [190, 191]. Antimuscarinic effects might also be induced or modulated through other cell types, such as the bladder urothelium or by the central nervous system [192, 193].

The following muscarinic receptor antagonists are licensed for treating OAB/storage symptoms: darifenacin hydrobromide (darifenacin); fesoterodine fumarate (fesoterodine); oxybutynin hydrochloride (oxybutynin); propiverine hydrochloride (propiverine); solifenacin succinate (solifenacin); tolterodine tartrate (tolterodine); and trospium chloride. Transdermal preparations of oxybutynin have been formulated and evaluated in clinical trials [194, 195].

Efficacy: Antimuscarinics were mainly tested in females in the past, as it was believed that LUTS in men were caused by the prostate, so should be treated with prostate-specific drugs. However, there is no scientific data for this assumption [196]. A sub-analysis of an open-label trial of OAB patients showed that age, but

not gender had an impact on urgency, frequency, or urgency incontinence [197]. In a pooled analysis, which included a sub-analysis of male patients, fesoterodine 8 mg was superior to tolterodine extended release (ER) 4 mg for the improvement of severe urgency episodes/24 hours and the OAB-q Symptom Bother score at week twelve, the urinary retention rate was around 2% [198].

The efficacy of antimuscarinics as single agents in men with OAB in the absence of BOO have been tested [199-204]. Most trials lasted only twelve weeks. Four *post hoc* analyses of large RCTs on the treatment of OAB in women and men without presumed BOO were performed focusing only on the men [196, 200, 205]. Tolterodine can significantly reduce urgency incontinence, daytime or 24-hour frequency and urgency-related voiding whilst improving patient perception of treatment benefit [206]. Solifenacin significantly improved mean patient perception of bladder condition scores, mean OAB questionnaire scores, and overall perception of bladder problems. Fesoterodine improved micturition frequency, urgency episodes, and UUI episodes. In open-label trials with tolterodine, daytime frequency, nocturia, UUI, and IPSS were significantly reduced compared with baseline values after twelve to 25 weeks [201, 204]. The TIMES RCT reported that tolterodine ER monotherapy significantly improved UUI episodes per 24 hours compared to placebo, at week twelve. Tolterodine ER did not significantly improve urgency, IPSS total or QoL score compared with placebo [203].

A further analysis showed that men with PSA levels of < 1.3 ng/mL (smaller prostates) might benefit more from antimuscarinics [207]. Two other studies found a positive effect of antimuscarinics in patients with OAB and concomitant BPO [204, 208]. In a small RCT propiverine improved frequency and urgency episodes [208].

Tolerability and safety: Antimuscarinic drug trials generally show approximately 3-10% withdrawals, which is similar to placebo. Drug-related adverse events include dry mouth (up to 16%), constipation (up to 4%), micturition difficulties (up to 2%), nasopharyngitis (up to 3%), and dizziness (up to 5%).

Increased PVR in men without BOO is minimal and similar to placebo. Nevertheless, fesoterodine 8 mg showed higher PVRs (+20.2 mL) than placebo (-0.6 mL) or fesoterodine 4 mg (+9.6 mL) [201]. Incidence of urinary retention in men without BOO was similar to placebo for tolterodine (0-1.3% vs. 0-1.4%). With fesoterodine 8 mg, 5.3% had symptoms, which was higher than placebo or fesoterodine 4 mg (both 0.8%). These symptoms appeared during the first two weeks of treatment and mainly affected men aged 66 years or older.

Theoretically antimuscarinics might decrease bladder strength, and hence might be associated with PVR or urinary retention. A twelve week safety study on men with mild-to-moderate BOO showed that tolterodine increased the PVR (49 mL vs. 16 mL) but not AUR (3% in both arms) [209]. The urodynamic effects included larger bladder volumes at first detrusor contraction, higher maximum cystometric capacity, and decreased bladder contractility index, Q_{max} was unchanged. This trial indicated that short-term treatment with antimuscarinics in men with BOO is safe [196].

Practical considerations: Not all antimuscarinics have been tested in elderly men, and long-term studies on the efficacy of muscarinic receptor antagonists in men of any age with LUTS are not yet available. In addition, only patients with low PVR volumes at baseline were included in the studies. These drugs should therefore be prescribed with caution, and regular re-evaluation of IPSS and PVR is advised. Men should be advised to discontinue medication if worsening voiding LUTS or urinary stream is noted after initiation of therapy.

Summary of evidence	**LE**
Antimuscarinic monotherapy can significantly improve urgency, UUI, and increased daytime frequency.	2
Antimuscarinic monotherapy can be associated with increased PVR after therapy, but acute retention is a rare event in men with a PVR volume of < 150 mL at baseline.	2

Recommendations	**Strength rating**
Use muscarinic receptor antagonists in men with moderate-to-severe LUTS who mainly have bladder storage symptoms.	Strong
Do not use antimuscarinic overactive bladder medications in men with a post-void residual volume > 150 mL.	Weak

5.2.4 ***Beta-3 agonist***

Mechanism of action: Beta-3 adrenoceptors are the predominant beta receptors expressed in the smooth muscle cells of the detrusor and their stimulation is thought to induce detrusor relaxation. The mode of action of beta-3 agonists is not fully elucidated [210].

Efficacy: Mirabegron 50 mg is the first clinically available beta-3 agonist with approval for use in adults with OAB. Mirabegron has undergone extensive evaluation in RCTs conducted in Europe, Australia, North America, and Japan [211-215]. Mirabegron demonstrated significant efficacy in treating the symptoms of OAB, including micturition frequency, urgency and UUI and also patient perception of treatment benefit. These studies had a predominantly female study population. A meta-analysis of eight RCTs including 10,248 patients (27% male) found that mirabegron treatment resulted in reduced frequency, urgency and UUI rates, as well as an improved voided volume with a statistically significant improvement of nocturia compared with both placebo and tolterodine [216].

Mirabegron has been evaluated in male patients with OAB in the context of LUTS either associated or not associated with BPO confirmed by urodynamics [217]. Mirabegron 25 mg daily led to increased satisfaction and improved QoL, but symptoms assessed by validated questionnaires (IPSS and OAB-SS), only improved in non-obstructed patients. Mirabegron as an add-on therapy has been studied in OAB patients with incontinence despite antimuscarinic therapy [218], again in a predominantly female study population. An Asian study with a higher proportion of male subjects (approximately one third) reported superiority over placebo in reducing frequency of micturition but did not report the results separately for the genders [219].

In a study of more than 1,000 patients of whom approximately 30% were male, combination therapy of mirabegron 25/50 mg and solifenacin 5/10 mg was associated with statistically significant improvements in patient outcomes and health related QoL vs. solifenacin 5 mg and placebo; however, they did not separate out the effects in men and women [220]. In another study, in which 28% patients were male, mirabegron significantly improved patient reported perception of their condition and QoL whether or not patients were incontinent [221]. A phase IV study, with a small proportion of male subjects, reported addition of mirabegron in people with persisting urgency despite solifenacin in a Japanese population [222].

Tolerability and safety: The most common treatment-related adverse events in the mirabegron groups were hypertension, UTI, headache and nasopharyngitis [211-214]. Mirabegron is contraindicated in patients with severe uncontrolled hypertension (systolic blood pressure ≥ 180 mmHg or diastolic blood pressure ≥ 110 mmHg, or both). Blood pressure should be measured before starting treatment and monitored regularly during treatment. A combination of thirteen clinical studies including 13,396 patients, 25% of whom were male, showed that OAB treatments (anticholinergics or mirabegron) were not associated with an increased risk of hypertension or cardiovascular events compared to placebo [223]. The proportion of patients with dry mouth and constipation in the mirabegron groups was notably lower than reported in RCTs of other OAB agents or of the active control tolterodine [211]. Evaluation of urodynamic parameters in men with combined BOO and OAB concluded that mirabegron did not adversely affect voiding urodynamic parameters compared to placebo in terms of Q_{max}, detrusor pressure at maximum flow and bladder contractility index [224]. The overall change in PVR with mirabegron is small [224].

A small prospective study (mainly focused on males) has shown that mirabegron 25 mg is safe in patients aged 80 years or more with multiple co-morbidities [225]. A pooled analysis of three trials, each of twelve weeks and a one-year trial showed, in patients aged > 65 years, a more favourable tolerability profile for mirabegron than antimuscarinics [226]. The PILLAR phase IV study also showed that in a large population of 888 patients ≥ 65 years (approx. 30% of males), mirabegron 50 mg was safe and effective [227]. In an eighteen-week study of 3,527 patients (23% male), the incidence of adverse events was higher in the combination (solifenacin 5 mg plus mirabegron 25 mg) group (40%) than the mirabegron 25 mg alone group (32%). Events recorded as urinary retention were low (< 1%) but were reported slightly more frequently in the combined group when compared with the monotherapy and placebo groups. The PVR volume was slightly increased in the combined group compared with solifenacin 5 mg, and the mirabegron monotherapy and placebo groups. Combined therapy with solifenacin 5 mg plus mirabegron 25 mg and solifenacin 5 mg plus mirabegron 50 mg provided improvements in efficacy generally consistent with an additive effect [228].

In a retrospective analysis of persistence and adherence in 21,996 patients, of whom 30% were male, the median time to discontinuation was significantly longer for mirabegron (169 days) compared to tolterodine (56 days) and other antimuscarinics (30-78 days). There was no statistical difference between men and women [229].

The phase III EMPOWUR trial comparing vibegron to placebo and tolterodine showed once daily 75 mg vibegron provided statistically significant reductions in micturitions, urgency episodes and UUI [230]. Treatment was well tolerated with a favourable safety profile. However, the majority of the study population (85%) were female and vibegron is not yet licenced in Europe.

Practical considerations: Long-term studies on the efficacy and safety of mirabegron in men of any age with LUTS are not yet available. Available studies on mirabegron in combination with antimuscarinics in OAB patients had a predominantly female study population, while further trials are still pending.

Summary of evidence	LE
Mirabegron improves storage LUTS, including urinary frequency, urgency and UUI.	2
Patients prescribed mirabegron remained on treatment longer than those prescribed antimuscarinics.	3

Recommendation	Strength rating
Use beta-3 agonists in men with moderate-to-severe LUTS who mainly have bladder storage symptoms.	Weak

5.2.5 Phosphodiesterase 5 inhibitors

Mechanism of action: Phosphodiesterase 5 inhibitors (PDE5Is) increase intracellular cyclic guanosine monophosphate, thus reducing smooth muscle tone of the detrusor, prostate, and urethra. Nitric oxide and PDE5Is might also alter reflex pathways in the spinal cord and neurotransmission in the urethra, prostate, or bladder [231]. Moreover, chronic treatment with PDE5Is seems to increase blood perfusion and oxygenation in the LUT [232]. Phosphodiesterase 5 inhibitors could also reduce chronic inflammation in the prostate and bladder [233]. The exact mechanism of PDE5Is on LUTS remains unclear.

Although clinical trials of several selective oral PDE5Is have been conducted in men with LUTS, only tadalafil (5 mg once daily) has been licensed for the treatment of male LUTS.

Efficacy: Randomised controlled trials have demonstrated that PDE5Is reduce IPSS, storage and voiding LUTS, and improve QoL. However, Q_{max} did not significantly differ from placebo in most trials [234]. A Cochrane review included a total of sixteen RCTs that examined the effects of PDE5Is compared to placebo and other standard of care drugs (α1-blockers and 5-ARIs) in men with LUTS [235]. In the updated meta-analysis, PDE5Is led to a small reduction (mean difference (MD) 1.89 lower; 95% CI: 2.27 lower to 1.50 lower; n = 4293) in IPSS compared to placebo [235]. There was no difference between PDE5Is and α1-blockers in IPSS [236]. Most evidence was limited to short-term treatment up to twelve weeks. In other meta-analyses, PDE5Is were also found to improve IPSS and IIEF score, but not always Q_{max} [237, 238]. A meta-regression suggested that younger men with low body mass index and more severe LUTS benefit the most from treatment with PDE5Is [237].

In a *post hoc* analysis of data pooled from four blinded trials of tadalafil 5 mg vs. placebo once daily, a minimum improvement of 25% in IPSS score was found in 60% in the tadalafil and in 44% in the placebo group [239]. The maximum trial duration was 52 weeks [240]. A subgroup analysis of pooled data from four RCTs demonstrated a significant reduction in LUTS, regardless of baseline severity, age, previous use of α-blockers or PDE5Is, total testosterone level or predicted prostate volume [241]. In a *post hoc* analysis of pooled data from four RCTs, tadalafil was shown to also be effective in men with cardiovascular risk factors/ co-morbidities, except for patients receiving more than one antihypertensive medication. Among sexually active men > 45 years, tadalafil improved both LUTS/BPH and ED [241].

An integrated data analyses from four placebo controlled clinical studies showed that total IPSS improvement was largely attributed to direct (92.5%) vs. indirect (7.5%) treatment effects via IIEF-EF improvement [242]. Another analysis showed a small but significant increase in Q_{max} without any effect on PVR [243]. An integrated analysis of RCTs showed that tadalafil was not superior to placebo for IPSS improvement at twelve weeks in men ≥ 75 years (with varied effect size between studies) but was for men < 75 years [244]. An open label urodynamic study of 71 patients showed significant improvements in both voiding and storage symptoms, confirmed by improvements in BOO index (61.3 to 47.1), and resolution of DO in fifteen (38%) of 38 patients. Flow rate improved from 7.1 to 9.1 mL/s and mean IPSS from 18.2 to 13.4 [245].

A multicenter, double blind, placebo controlled RCT compared once daily tadalafil 20 mg vs. placebo during twelve weeks in men with LUTS with or without BOO. Urodynamic measures including detrusor pressure at maximum urinary flow rate, Q_{max}, maximum detrusor pressure, BOO or bladder capacity remained largely unchanged during the study with no statistically significant or clinically adverse event differences between tadalafil and placebo [246].

A combination of PDE5Is and α-blockers has also been evaluated. A meta-analysis of five RCTs (two studies with tadalafil 20 mg, two with sildenafil 25 mg, and one with vardenafil 20 mg), showed that combination therapy significantly improved IPSS score (-1.8), IIEF score (+3.6) and Q_{max} (+1.5 mL/s) compared with α-blockers alone [237]. Both a SR and Cochrane review found similar findings [235, 247]. The effects of tadalafil 5 mg combined with finasteride 5 mg were assessed in a 26-week placebo-controlled RCT. The combination of tadalafil and finasteride provided a significant early improvement in urinary symptoms at four, twelve and 26 weeks as well as a significant improvement of storage and voiding symptoms and QoL. Combination therapy was well tolerated and improved erectile function [248]. However, only tadalafil 5 mg has been licensed in the context of LUTS management while data on combinations of PDE5Is and other LUTS medications is emerging.

Tolerability and safety: Reported adverse effects in RCTs comparing the effect of all PDE5Is vs. placebo in men with LUTS include flushing, gastroesophageal reflux, headache, dyspepsia, back pain and nasal congestion [237].

Tadalafil is contraindicated in patients using nitrates or guanylate cyclase stimulators, such as riociguat, and in men with cardiac disease for whom sexual activity is inadvisable [249]. Tadalafil is also contraindicated in patients with myocardial infarction within the last 90 days, - patients with unstable angina or angina occurring during sexual intercourse, - patients with New York Heart Association Class 2 or greater heart failure in the last six months, - patients with uncontrolled arrhythmias, hypotension (< 90/50 mm Hg), or uncontrolled hypertension, - patients with a stroke within the last six months or if anterior ischaemic optic neuropathy with sudden loss of vision is known or was reported after previous use of PDE5Is [249]. Detailed information regarding tolerability/safety of all available PDE5Is for the treatment of erectile dysfunction in men treated with α-blockers for LUTS are provided by the EAU Guidelines on Sexual and Reproductive Health [250].

Practical considerations: To date, only tadalafil 5 mg once daily has been officially licensed for the treatment of male LUTS with or without ED. Long-term experience with tadalafil in men with LUTS is limited to one trial with a one-year follow-up [240]; limiting conclusions about efficacy or tolerability greater than one year. There is limited information on reduction of prostate size and no data on disease progression.

Summary of evidence	LE
Phosphodiesterase 5 inhibitors significantly improve IPSS and IIEF score, but not Q_{max}.	1a

Recommendation	Strength rating
Use phosphodiesterase type 5 inhibitors in men with moderate-to-severe LUTS with or without erectile dysfunction.	Strong

5.2.6 *Plant extracts - phytotherapy*

Potential mechanism of action: Herbal drug preparations are made of roots, seeds, pollen, bark, or fruits. There are single plant preparations (mono-preparations) and preparations combining two or more plants in one pill (combination preparations) [251].

Possible relevant compounds include phytosterols, ß-sitosterol, fatty acids, and lectins [251]. *In vitro*, plant extracts can have anti-inflammatory, anti-androgenic and oestrogenic effects; decrease sexual hormone binding globulin; inhibit aromatase, lipoxygenase, growth factor-stimulated proliferation of prostatic cells, α-adrenoceptors, 5 α-reductase, muscarinic acetylcholine receptors, dihydropyridine receptors and vanilloid receptors; and neutralise free radicals [245, 251, 252]. The *in vivo* effects of these compounds are uncertain, and the precise mechanisms of plant extracts remain unclear.

Efficacy: The extracts of the same plant produced by different companies do not necessarily have the same biological or clinical effects; therefore, the effects of one brand cannot be extrapolated to others [253]. In addition, batches from the same producer may contain different concentrations of active ingredients [254]. A review of recent extraction techniques and their impact on the composition/biological activity of available *Serenoa repens* based products showed that results from different clinical trials must be compared strictly according to the same validated extraction technique and/or content of active compounds [255], as the pharmacokinetic properties of the different preparations can vary significantly.

Heterogeneity and a limited regulatory framework characterise the current status of phytotherapeutic agents. The European Medicines Agency (EMA) has developed the Committee on Herbal Medicinal Products (HMPC). European Union (EU) herbal monographs contain the HMPC's scientific opinion on safety and efficacy data about herbal substances and their preparations intended for medicinal use. The HMPC evaluates all available information, including non-clinical and clinical data, whilst also documenting long-standing use and experience in the EU. European Union monographs are divided into two sections: a) Well established use (marketing authorisation): when an active ingredient of a medicine has been used for more than ten years and its efficacy and safety have been well established (including a review of the relevant literature); and b) Traditional use (simplified registration): for herbal medicinal products which do not fulfil the requirements for a marketing authorisation, but there is sufficient safety data and plausible efficacy on the basis of long-standing use and experience.

The HPMC periodically invites all interested parties to submit any scientific data that the Committee should consider during their periodic review of the monographs. Table 1 lists the available EU monographs for herbal medicinal products and the current calls for update.

Table 1: European Union monographs for herbal medicinal products [256]

Herbal substance	HMPC evaluation	Therapeutic Indication by HMPC	Date of monograph
Serenoa repens, fructus (saw palmetto, fruit) Extraction solvent: hexane [257]	Well established use	Symptomatic treatment of BPH	14/01/2016 Addendum 1/9/21**
Serenoa repens, fructus (saw palmetto, fruit) Extraction solvent: ethanol [257]	Traditional use	LUTS related to BPH*	14/01/2016 Addendum 1/9/21**
Cucurbita pepo L, semen (pumpkin seed) Preparation as defined in the monograph [258]	Traditional use	LUTS related to BPH or related to an OAB*	25/03/2013 Call ended 30/4/21
Prunus africana (Hook f.) Kalkm., cortex (pygeum africanum bark) Preparation as defined in the monograph [259]	Traditional use	LUTS related to BPH*	01/09/2017 No call for update
Urtica dioica L., Urtica urens L., their hybrids or their mixtures, radix Preparation as defined in the monograph [260]	Traditional use	LUTS related to BPH*	05/11/2012 Call ended 30/6/21
Epilobium angustifolium L. and/or *Epilobium parviflorum Schreb., herba (Willow herb)* Preparation as defined in the monograph [261]	Traditional use	LUTS related to BPH*	13/01/2016 No call for update

** After serious conditions have been excluded by a medical doctor.*

*** Addendum concluded that no revision was needed.*

Panel interpretation: Only hexane extracted Serenoa repens (HESr) has been recommended for well-established use by the HMPC. Based on this a detailed scoping search covering the timeframe between the search cut-off date of the EU monograph and May 2021 was conducted for HESr.

A large meta-analysis of 30 RCTs with 5,222 men and follow-up ranging from four to 60 weeks, demonstrated no benefit of treatment with *S. repens* in comparison to placebo for the relief of LUTS [262]. It was concluded that *S. repens* was not superior to placebo, finasteride, or tamsulosin with regard to IPSS improvement, Q_{max}, or prostate size reduction; however, the similar improvement in IPSS or Q_{max} compared with finasteride or tamsulosin could be interpreted as treatment equivalence. Importantly, in the meta-analysis all different brands of *S. repens* were included regardless or not of the presence of HESr as the main ingredient in the extract.

Another SR focused on data from twelve RCTs on the efficacy and safety of HESr [263]. It was concluded that HESr was superior to placebo in terms of improvement of nocturia and Q_{max} in patients with enlarged prostates. Improvement in LUTS was similar to tamsulosin and short-term use of finasteride. An updated SR analysed fifteen RCTs and also included twelve observational studies. It confirmed the results of the previous SR on the efficacy of HESr [264]. Compared with placebo, HESr was associated with 0.64 (95% CI: 0.98 - 0.31) fewer voids/night and an additional mean increase in Q_{max} of 2.75 mL/s (95% CI: 0.57 - 4.93), both were significant. When compared with α-blockers, HESr showed similar improvements in IPSS (WMD 0.57; 95% CI: 0.27 - 1.42) and a comparable increase in Q_{max} when compared to tamsulosin (WMD 0.02; 95% CI: 0.71 - 0.66). Efficacy assessed using IPSS was similar after six months of treatment between HESr and 5-ARIs. Analysis of all available published data for HESr showed a mean significant improvement in IPSS from baseline of 5.73 points (95% CI: 6.91 - 4.54) [264].

A network meta-analysis tried to compare the clinical efficacy of *S. repens* (HESr and non-HESr) against placebo and α1-blockers in men with LUTS. Interestingly, only two RCTs on HESr were included in the analysis. It was found that *S. repens* achieved no clinically meaningful improvement against placebo or α1-blockers in short-term follow-up. However, *S. repens* showed a clinical benefit after a prolonged period of treatment, and HESr demonstrated a greater improvement than non-HESr in terms of IPSS [265].

With respect to safety and tolerability data from the SRs showed that HESr had a favourable safety profile with gastrointestinal disorders being the most frequent adverse effects (mean incidence 3.8%) while HESr had very limited impact on sexual function.

A cross-sectional study compared the combination of HESr with silodosin, to silodosin monotherapy in patients treated for at least twelve months (mean duration 13.5 months) [266]. It was reported that 69.9% of the combination therapy patients achieved the predefined clinically meaningful improvement (improvement more than three points in baseline IPSS) compared to 30.1% of patients treated only with silodosin. In addition, a greater than 25% improvement in IPSS was found in 68.8% and 31.2% of the patients in the combination and the monotherapy groups, respectively. These data suggest that combination of a α1-blocker with HESr may result in greater clinically mean-ingful improvements in LUTS compared to α1-blocker monotherapy [266].

Practical considerations: Available RCTs do not use the same endpoints (e.g., IPSS). More studies on the use of HESr in combination with other pharmacotherapeutic agents for male LUTS are pending. There is a need to define the subpopulation of patients who will benefit most from therapy with HESr.

Summary of evidence	LE
Hexane extracted *Serenoa repens* improves Q_{max} and results in fewer voids/night (0.64 [95% CI: 0.98 to 0.31]) compared to placebo.	2
Hexane extracted *Serenoa repens* has a very limited negative impact on sexual function.	2

Recommendations	Strength rating
Offer hexane extracted *Serenoa repens* to men with LUTS who want to avoid any potential adverse events especially related to sexual function.	Weak
Inform the patient that the magnitude of efficacy may be modest.	Strong

*5.2.7 **Combination therapies***

5.2.7.1 Alpha 1-blockers + 5 Alpha reductase inhibitors

Mechanism of action: Combination therapy consists of an α1-blocker (Section 5.2.1) together with a 5-ARI (Section 5.2.2). The α1-blocker exhibits clinical effects within hours or days, whereas the 5-ARI needs several months to develop full clinical efficacy. Finasteride has been tested in clinical trials with alfuzosin, terazosin, doxazosin or terazosin, and dutasteride with tamsulosin.

Efficacy: Several studies have investigated the efficacy of combination therapy against an α1-blocker, 5-ARI, or placebo alone. Initial studies with follow-up periods of six to twelve months demonstrated that the α1-blocker was superior to finasteride in symptom reduction, whereas combination therapy of both agents was not superior to α1-blocker monotherapy [167, 168, 267]. In studies with a placebo arm, the α1-blocker was consistently more effective than placebo, but finasteride was not. Data at one year in the MTOPS study showed similar results [65].

Long-term data (four years) from the MTOPS and CombAT studies showed that combination treatment is superior to monotherapy for symptoms and Q_{max}, and superior to α1-blocker alone in reducing the risk of AUR or need for surgery [65, 151, 152].

The CombAT study demonstrated that combination treatment is superior to either monotherapy regarding symptoms and flow rate starting from month nine, and superior to α1-blocker for AUR and the need for surgery after eight months [152]. Thus, the differences in MTOPS may reflect different inclusion and exclusion criteria and baseline patient characteristics.

Discontinuation of the α1-blocker after six to nine months of combination therapy was investigated in an RCT and an open-label multicentre trial [268, 269]. The first trial evaluated the combination of tamsulosin with dutasteride and the impact of tamsulosin discontinuation after six months [268], with almost three quarters of patients reporting no worsening of symptoms. However, patients with severe symptoms (IPSS > 20) at baseline may benefit from longer combination therapy.

A more recent trial evaluated the symptomatic outcome of finasteride monotherapy at three and nine months after discontinuation of nine-month combination therapy [269]. Lower urinary tract symptom improvement after combination therapy was sustained at three months (IPSS difference 1.24) and nine months (IPSS difference 0.4). The limitations of the studies include the short duration of the studies and the short follow-up period after discontinuation.

In both the MTOPS and CombAT studies, combination therapy was superior to monotherapy in preventing clinical progression as defined by an IPSS increase of at least four points, AUR, UTI, incontinence, or an increase in creatinine > 50%. The MTOPS study found that the risk of long-term clinical progression (primarily due to increasing IPSS) was reduced by 66% with combined therapy vs. placebo and to a greater extent than with either finasteride or doxazosin monotherapy (34% and 39%, respectively) [65]. In addition, finasteride

(alone or in combination), but not doxazosin alone, significantly reduced both the risks of AUR and the need for BPO-related surgery over the four-year study. In the CombAT study, combination therapy reduced the relative risks of AUR by 68%, BPO-related surgery by 71%, and symptom deterioration by 41% compared with tamsulosin, after four years [270]. To prevent one case of urinary retention and/or surgical treatment, thirteen patients need to be treated for four years with dutasteride and tamsulosin combination therapy compared to tamsulosin monotherapy while the absolute risk reduction (risk difference) was 7.7%.

The CONDUCT study compared efficacy and safety of a fixed-dose combination of dutasteride and tamsulosin to a WW approach with the potential initiation of tamsulosin (step-up approach) in a two-year RCT with a total of 742 patients. In both arms detailed lifestyle advice was given. This fixed-dose combination resulted in a rapid and sustained improvement in men with moderate LUTS at risk of disease progression, the difference in IPSS at 24 months was 5.4 in the active arm and 3.6 in the placebo arm [271]. Furthermore, tamsulosin plus dutasteride significantly reduced the relative risk of clinical progression (mainly characterised as a worsening in symptoms) by 43.1% when compared with WW, with an absolute risk reduction of 11.3% (number needed to treat [NNT] = 9).

The influence of baseline variables on changes in IPSS after combination therapy with dutasteride plus tamsulosin or either monotherapy was tested based on the four-year results of the CombAT study. Combination therapy provided consistent improvement of LUTS over tamsulosin across all analysed baseline variables at 48 months [272].

A combination of the 5-ARI finasteride and tadalafil 5 mg was tested in a large scale RCT against finasteride monotherapy. This study supports the concept of this novel combination therapy and is described in more detail in section 5.2.5 [248].

Tolerability and safety: Adverse events for both drug classes have been reported with combination treatment [65, 151, 152]. The adverse events observed during combination treatment were typical of α1-blockers and 5-ARIs. The frequency of adverse events was significantly higher for combination therapy. The MTOPS study demonstrated that the incidence of treatment related adverse events is higher during the first year of combined treatment between doxazosin and finasteride [273]. A meta-analysis measuring the impact of medical treatments for LUTS/BPH on ejaculatory function, reported that combination therapy with α1-blockers and 5-ARIs resulted in a three-fold increased risk of EjD compared with each monotherapy [162].

Practical considerations: Compared with α1-blockers or 5-ARI monotherapy, combination therapy results in a greater improvement in LUTS and increase in Q_{max} and is superior in prevention of disease progression. However, combination therapy is also associated with a higher rate of adverse events. Combination therapy should therefore be prescribed primarily in men who have moderate-to-severe LUTS who are at risk of disease progression (higher prostate volume, higher PSA concentration, advanced age, higher PVR, lower Q_{max}, etc.). Combination therapy should only be used when long-term treatment (more than twelve months) is intended, and patients should be informed of this. Discontinuation of the α1-blocker after six months might be considered in men with moderate LUTS.

Summary of evidence	**LE**
Long-term data (four years) from the MTOPS and CombAT studies showed that combination treatment is superior to monotherapy for symptoms and Q_{max}, and superior to α1-blocker alone in reducing the risk of AUR or need for surgery.	1b
The MTOPS study found that the risk of long-term clinical progression (primarily due to increasing IPSS) was reduced by 66% with combined therapy vs. placebo and to a greater extent than with either finasteride or doxazosin monotherapy.	1b
The CombAT study found that combination therapy reduced the relative risks of AUR by 68%, BPH-related surgery by 71%, and symptom deterioration by 41% compared with tamsulosin, after four years.	1b
Adverse events of both drug classes are seen with combined treatment using α1-blockers and 5-ARIs.	1b

Recommendation	**Strength rating**
Offer combination treatment with an α1-blocker and a 5α-reductase inhibitor to men with moderate-to-severe LUTS and an increased risk of disease progression (e.g. prostate volume > 40 mL).	Strong

5.2.7.2 Alpha 1-blockers + muscarinic receptor antagonists

Mechanism of action: Combination treatment consists of an α1-blocker together with an antimuscarinic aiming to antagonise both α1-adrenoceptors and muscarinic receptors. The possible combinations have not all been tested in clinical trials to date.

Efficacy: Several RCTs and prospective studies investigated combination therapy, lasting four to twelve weeks, either as an initial treatment in men with OAB and presumed BPO or as a sequential treatment for storage symptoms persisting while on an α1-blocker [195, 206, 270, 274-281]. Combination treatment is more efficacious in reducing urgency, UUI, voiding frequency, nocturia, or IPSS compared with α1-blockers or placebo alone, and improves QoL [206, 281]. A SR showed that combination therapy of tolterodine and an α1-blocker was significantly more efficacious than either monotherapy for 24-hours and night voiding frequency, and 24-hours urgency episodes [206].

One trial used the α1-blocker naftopidil (not registered in most European countries) with and without antimuscarinics [282]. A high proportion of men with voiding and storage LUTS need to add anticholinergics after α1-blocker monotherapy, particularly those with longer duration of symptoms at presentation, and men with storage symptoms and a small prostate volume [283].

Symptom improvement is higher regardless of PSA concentration with combination therapy, whereas tolterodine alone improved symptoms mainly in men with a serum PSA of < 1.3 ng/mL [207].

Persistent LUTS during α1-blocker treatment can be reduced by the additional use of an antimuscarinic, [270, 274, 280, 284, 285]. Two SRs of the efficacy and safety of antimuscarinics in men suggested that combination treatment provides significant benefit [286, 287]. In a meta-analysis of sixteen studies with 3,548 patients with BPH/OAB, initial combination treatment of an α1-blocker with anticholinergic medication improvement storage symptoms and QoL compared to α1-blocker monotherapy without causing significant deterioration of voiding function [288]. There was no difference in total IPSS and Q_{max} between the two groups.

Effectiveness of therapy is evident primarily in those men with moderate-to-severe storage LUTS [289]. Long term use of combination therapy has been reported in patients receiving treatment for up to one year, showing symptomatic response is maintained, with a low incidence of AUR [290]. In men with moderate-to-severe storage symptoms, voiding symptoms and PVR < 150 mL, the reduction in symptoms using combination therapy is associated with patient-relevant improvements in health related QoL compared with placebo and α1-blocker monotherapy [291].

The intake of fixed-dose combination tablet containing solifenacin 6 mg and tamsulosin 0.4 mg improved OAB-q symptom bother in > 80% of LUTS/BPH patients not adequately responding to monotherapy, with a high treatment persistence (77% at weeks 40 to 52), and a low risk of AUR [292]. Combined behavioural and drug therapy yielded greater improvements in OAB symptoms than drug therapy alone, but not behavioural therapy alone in a RCT evaluating the effectiveness of combined behavioural strategies and drug therapy for OAB symptoms in men [293].

Tolerability and safety: Adverse events of both drug classes are seen with combined treatment using α1-blockers and antimuscarinics. The most common side-effect is dry mouth. Some side-effects (e.g. dry mouth or ejaculation failure) may show increased incidence which cannot simply be explained by summing the incidence with the drugs used separately. Increased PVR may be seen, but is usually not clinically significant, and risk of AUR is low up to one year of treatment [203, 286, 294]. Antimuscarinics do not cause evident deterioration in Q_{max} used in conjunction with an α1-blocker in men with OAB symptoms [281, 295].

A recent RCT investigated safety in terms of maximum detrusor pressure and Q_{max} for solifenacin (6 mg or 9 mg) with tamsulosin in men with LUTS and BOO compared with placebo [296]. The combination therapy was non-inferior to placebo for the primary urodynamic variables; Q_{max} was increased vs. placebo [296].

Practical considerations: Class effects are likely to underlie efficacy and QoL using an α1-blocker and antimuscarinic. Trials used mainly storage symptom endpoints, were of short duration, and included only men with low PVR volumes at baseline. Therefore, measuring PVR is recommended during combination treatment.

Summary of evidence	**LE**
Combination treatment with α1-blockers and antimuscarinics is effective for improving LUTS-related QoL impairment.	2
Combination treatment with α1-blockers and antimuscarinics is more effective for reducing urgency, UUI, voiding frequency, nocturia, or IPSS compared with α1-blockers or placebo alone.	2
Adverse events of both drug classes are seen with combined treatment using α1-blockers and antimuscarinics.	1

There is a low risk of AUR using α1-blockers and antimuscarinics in men known to have a PVR volume of < 150 mL.	2

Recommendations	Strength rating
Use combination treatment of a α1-blocker with a muscarinic receptor antagonist in patients with moderate-to-severe LUTS if relief of storage symptoms has been insufficient with monotherapy with either drug.	Strong
Do not prescribe combination treatment in men with a post-void residual volume > 150 mL.	Weak

5.2.7.3 Alpha 1-blockers + beta-3 agonist

Mechanism of action: Combination therapy consists of an α1-blocker (Section 5.2.1) together with a beta-3-agonist (Section 5.2.4) as an add-on therapy in males receiving α1-blockers with persisting OAB symptoms.

Efficacy: The MATCH study explored the effect of the addition of mirabegron 50 mg to tamsulosin 0.2 mg compared to tamsulosin plus placebo in 544 patients [297]. A statistically significant difference of 0.52 voids per day was seen in favour of mirabegron. Total IPSS score also improved but was not significant between the groups. Another RCT evaluated add-on therapy with mirabegron for OAB symptoms persisting after treatment with tamsulosin 0.2 mg daily in men with BPO [298]. Combination therapy was associated with greater improvements in OAB symptom score, in urinary urgency and daytime frequency as well as the storage sub-score of IPSS and QoL index compared to monotherapy with tamsulosin [299].

The PLUS phase IV trial [298] compared mirabegron and placebo in a population of males treated with a standard dose of tamsulosin 0.4 mg. After a four-week run-in period of treatment with tamsulosin 0.4 mg alone, 715 patients were randomised between placebo and mirabegron 25 mg, upgraded to 50 mg after one month. While mean number of micturition's were significantly reduced in the experimental arm, the effect size was deemed as low (mean adjusted difference of 0.39 voids per day). Similar results were seen for mean voided volume and urgency episodes, but total IPSS, IPSS sub-scores and OAB-q symptom score were not significantly different between the groups.

An RCT comparing the efficacy of mirabegron 50 mg or fesoterodine 4 mg add-on therapy to silodosin in LUTS patients with persisting OAB symptoms reported that at three months, fesoterodine add-on therapy showed a significantly greater improvement than mirabegron add-on therapy in OAB symptom score and urgency score and IPSS-QoL score [220]. Fesoterodine was also superior in alleviating DO.

Tolerability and safety: In the MATCH study main adverse events were in line with previous trials, and cardiovascular events were uncommon in the studied populations [297]. The PLUS phase IV trial also reported adverse events similar to those seen in previous trials (hypertension, headache and nasopharyngitis being the most frequent) [298]. There were six episodes of retention recorded (1.7%) and overall, no clinically significant specific change was seen in Q_{max} and PVR. An open-label, randomised, 2-arm, 2-sequence study reported that the addition of mirabegron or tamsulosin to patients under tamsulosin or mirabegron mono therapy did not cause clinically relevant changes in cardiovascular safety or safety profiles [300].

Solifenacin and mirabegron were also compared in another RCT that has shown comparable efficacy but a better safety profile for mirabegron [301].

Practical considerations: Add-on therapy with mirabegron in patients with remaining symptoms under α1-blocker therapy has been evaluated only in short-term clinical trials. The short-term benefit remains uncertain with a low effect size in urinary frequency compared to placebo, and more studies with longer follow-up are required.

Summary of evidence	LE
Combination treatment with α1-blockers and mirabegron results in a slight decrease of number of voids and urgency episodes per day compared with α1-blockers alone.	1b
Adverse events of both drug classes are seen with combined treatment using α1-blockers and mirabegron.	1b

Recommendations	Strength rating
Use combination treatment of a α1-blocker with mirabegron in patients with persistent storage LUTS after treatment with α1-blocker monotherapy.	Weak

Note: All patients should be counselled about pharmacological treatment related adverse events in order to select the most appropriate treatment for each individual patient.

5.3 Surgical treatment

Surgical treatment is one of the cornerstones of LUTS/BPO management. Based on its ubiquitous availability, as well as its efficacy, monopolar TURP (M-TURP) has long been considered as the reference technique for the surgical management of LUTS/BPO. However, in recent years various techniques have been developed with the aim of providing a safe and effective alternative to M-TURP. Previously, the surgical section of the Guidelines was based on technology rather than surgical approach. As the clinical reality is primarily reflected by surgical approach and not necessarily by a specific technology, the chapter on surgical management has been restructured. It is now divided into the following five sections:

1. Resection;
2. Enucleation;
3. Vaporisation;
4. Alternative ablative techniques; and
5. Non-ablative techniques.

In addition, most of the studies are restricted by prostate size, which is also reflected in the present Guidelines. Notably, only a small fraction of RCTs are performed in patients with a prostate > 80 mL; therefore, high-level evidence for larger prostates are limited.

Based on Panel consensus, timeframes defining short-, mid- and long-term follow-up of patients submitted to surgical treatments are twelve, 36, and over 36 months, respectively. The durability of a technique is reflected by the re-operation rate during follow-up, the failure to wean patients off medication as well as the initiation of novel LUTS medication after surgery. However, for the majority of techniques only the re-operation rate is reported, and clinicians should inform patients that long-term surgical RCTs are often lacking. Some patients value sexual function and perceived higher safety over maximum efficacy and it is not therefore surprising that some patients consciously choose an alternative ablative or non-ablative technique despite the knowledge that it might not be their definitive treatment. In contrast, many urologists are critical about these procedures due to their inferior relief of BOO.

Recommendations on new devices or interventions will only be included in the Guidelines once supported by a minimum level of evidence. To clarify this the Panel have published their position on certainty of evidence (CoE) [302]. In summary, a device or technology is only included once supported by RCTs looking at both efficacy and safety, with adequate follow-up, and secondary studies to confirm the reproducibility and generalisability of the first pivotal studies [302]. Otherwise, there is a danger that a single pivotal study can be over exploited by device manufacturers. Studies that are needed include proof of concept, RCTs on efficacy and safety, as well as cohort studies with a broad range of inclusion and exclusion criteria to confirm both reproducibility and generalisability of the benefits and harms [302]. The panel assesses the quality of all RCTs and if they do not meet the standard required the intervention will continue to have no recommendation i.e., an RCT does not guarantee inclusion in the Guidelines.

In addition, the Guidelines continues to include techniques under investigation. These are devices or technologies that have shown promising results in initial studies; however, they do not meet the aforementioned criteria yet to provide a CoE which allows the Panel to regard these devices or technologies as recommended alternatives. To account for evolving evidence, recommendations for some techniques under investigation have been made; however, these techniques remain under investigation until further studies provide the recommended CoE.

*5.3.1 **Resection of the prostate***

5.3.1.1 Monopolar and bipolar transurethral resection of the prostate

Mechanism of action: Transurethral resection of the prostate is either performed in a M-TURP or bipolar TURP (B-TURP) fashion. Transurethral resection of the prostate removes tissue from the transition zone of the gland in various degrees resulting in a volume and PSA reduction of 25 -58%. Contrary to M-TURP, in B-TURP systems, the energy does not travel through the body to reach a skin pad. Bipolar circuitry is completed locally; energy is confined between an active (resection loop) and a passive pole situated on the resectoscope tip (“true” bipolar systems) or the sheath (“quasi” bipolar systems) using normal saline for irrigation thereby eliminating transurethral resection syndrome (TUR-syndrome) [303, 304].

Efficacy: In a meta-analysis of twenty RCTs with a maximum follow-up of five years, M-TURP resulted in a substantial mean Q_{max} improvement (+162%), a significant reduction in IPSS (-70%), QoL score (-69%), and PVR (-77%) [305]. Monopolar-TURP delivers durable outcomes as shown by studies with a follow-up of eight to 22 years [306]. One study with a mean follow-up of thirteen years reported a significant and sustained decrease in most symptoms and improvement in urodynamic parameters. Failures were associated with detrusor underactivity (DUA) rather than re-growth of BPH [103]. A second prostatic operation, usually

re-TURP, has been reported at a constant annual rate of approximately 1-2%. A SR analysing 29 RCTs found a retreatment rate of 2.6% after a mean follow-up of sixteen months [307]. Data from an Austrian nationwide study of two cohorts totalling 41,059 men submitted to M-TURP showed that the overall retreatment rates (re-TURP, urethrotomy and bladder neck incision) remained unchanged during the last decade (0.9%, 3.7%, 9.5% and 12.7% at three months, one year, five years, and eight years, respectively), and that the respective incidence of re-TURP was 0.8%, 2.4%, 6.1% and 8.3%, respectively [308, 309].

Bipolar TURP is the most widely investigated alternative to M-TURP. Pooled results from 59 RCTs have been reported to date [310]. Early pooled results as well as at twelve months, concluded that no clinically relevant differences exist in short-term efficacy (IPSS, QoL score and Q_{max}) [310, 311]. Subsequent meta-analyses supported these conclusions though trial quality was generally poor [305, 312-315]. The largest meta-analysis published to date, confirmed that B-TURP compared to M-TURP results in little to no difference in urological symptoms and bother (IPSS and QoL score) at twelve months [310]. Data from RCTs with mid- to long-term follow-up (up to 60 months) showed no differences in efficacy parameters [316-324]. A meta-analysis of RCTs comparing B-TURP vs. M-TURP, reported similar efficacy at 36 months in terms of IPSS, and Q_{max} [325].

A meta-analysis was conducted to evaluate the quasi-bipolar transurethral resection in saline (TURis), Olympus Medical system vs. M-TURP. Ten unique RCTs (1,870 patients) were included, and it was concluded that TURis was of equivalent efficacy to M-TURP [326].

Tolerability and safety: Peri-operative mortality and morbidity of M-TURP have decreased over time, but morbidity remains considerable (0.1% and 11.1%, respectively) [327]. Data from an Austrian nationwide study of two cohorts totalling 41,059 men submitted to M-TURP showed a 20% reduction in mortality rate over time, to 0.1% at 30 days and 0.5% at 90 days [308, 309].

The risk of TUR-syndrome decreased to < 1.1% [307, 328]. Data from 10,654 M-TURPs reported bleeding requiring transfusion in 2.9% [327]. Short- to mid-term complications reported in an analysis of RCTs using M-TURP as a comparator were: bleeding requiring transfusion 2% (0-9%), TUR-syndrome 0.8% (0-5%), AUR 4.5% (0-13.3%), clot retention 4.9% (0-39%), and UTI 4.1% (0-22%) [305]. Long-term complications of M-TURP comprise UI, urinary retention and UTIs, bladder neck contracture (BNC), urethral stricture, retrograde ejaculation and ED [307].

Early pooled results concluded that no differences exist in short-term urethral stricture/BNC rates, but B-TURP is preferable to M-TURP due to a more favourable peri-operative safety profile (elimination of TUR-syndrome; lower clot retention/blood transfusion rates; shorter irrigation, catheterisation, and possibly hospitalisation times) [311]. Subsequent meta-analyses supported these conclusions [305, 312-315, 325]; however, trial quality was relatively poor and limited follow-up might cause under-reporting of late complications, such as urethral stricture/BNC [311]. The largest meta-analysis published to date, concluded that B-TURP compared to M-TURP reduced TUR-syndrome and blood transfusion events by twenty and 28 fewer events per 1,000 participants, respectively [310]. The study also concluded that B-TURP may carry a similar risk of UI and may result in similar rates of re-TURP in the short-term (four fewer events and one more re-TURP per 1000 participants, respectively), compared to M-TURP [310]. An RCT based meta-analysis has shown that TURis reduces the risk of TUR-syndrome and the need for blood transfusion compared to M-TURP [315]. It was concluded that TURis is associated with improved peri-operative safety, eliminating the risk of TUR-syndrome, reducing the risk of blood transfusion/clot retention and hospital stay. No significant difference was detected in urethral stricture rates.

Data from the vast majority of individual RCTs with mid- to long-term follow-up (up to 60 months), showed no differences between M-TURP and B-TURP in urethral stricture/BNC rates [316-324], in accordance with all published meta-analyses. However, two individual RCTs have shown opposing results [323, 329]. A significantly higher stricture (urethral stricture + BNC) rate was detected in the B-TURP arm performed with a “quasi” bipolar system (TURis, Olympus Medical) in patients with a prostate volume > 70 mL at 36-months follow-up [323]. In addition, a significantly higher BNC, but not urethral stricture, rate was detected in the B-TURP arm performed with a “true” bipolar system (Gyrus PK SuperPulse, Olympus Medical) in 137 patients at twelve months follow-up [329].

Randomised controlled trials using the erectile function domain of the IIEF (IIEF-ED) and the ejaculatory domain of the male sexual-health questionnaire (Ej-MSHQ) showed that M-TURP and B-TURP have a similar effect on erectile and ejaculatory function [330, 331]. Comparative evaluations of the effects on overall sexual function, quantified with IIEF-15, showed no differences between B-TURP and M-TURP at twelve months follow-up (erection, orgasmic function, sexual desire, intercourse satisfaction, overall satisfaction) [331, 332]. Furthermore, the largest meta-analysis published to date, showed that erectile function measured by IIEF-5 appears to be similar at twelve months follow-up after B-TURP and M-TURP [310].

A comparative study [333] evaluated the safety of B-TURP in patients taking therapeutic oral anticoagulation (phenprocoumon) or anti-platelet drug therapy (acetylsalicylic acid or clopidogrel), without stopping or bridging the medication. Outcomes under acetylsalicylic acid were comparable to the unmedicated control group. Under oral anticoagulation therapy catheterisation (median 41-hours vs. 24-hours) and hospitalisation time was longer (median four days vs. three days), AUR rate was higher (18% vs. 6%), but blood transfusion rates did not differ to the control group. Under anti-platelet therapy blood transfusion (19% vs. 1%) and re-hospitalisation rates (19% vs. 3%) were higher.

Practical considerations: Monopolar-TURP is an effective treatment for moderate-to-severe LUTS secondary to BPO. The choice should be based primarily on prostate volume (30-80 mL suitable for M-TURP). No studies on the optimal cut-off value exist, but the complication rates increase with prostate size [327]. The upper limit for M-TURP is suggested as 80 mL (based on Panel consensus, under the assumption that this limit depends on the surgeon's experience, choice of resectoscope size and resection speed), as surgical duration increases, there is a significant increase in the rate of complications and the procedure is safest when performed in under 90 minutes [334].

Bipolar TURP in patients with moderate-to-severe LUTS secondary to BPO has similar efficacy with M-TURP but lower peri-operative morbidity. The duration of improvements with B-TURP were documented in a number of RCTs with mid-term follow-up. Long-term results (up to five years) for B-TURP showed that safety and efficacy are comparable to M-TURP [316-324]. The choice of B-TURP should be based on equipment availability, surgeon's experience, and patient's preference.

Summary of evidence	**LE**
Bipolar- or M-TURP is the current standard surgical procedure for men with prostate sizes of 30-80 mL and bothersome moderate-to-severe LUTS secondary of BPO.	1a
Bipolar-TURP achieves short-, mid- and long-term results comparable with M-TURP, but B-TURP has a more favourable peri-operative safety profile.	1a

Recommendation	**Strength rating**
Offer bipolar- or monopolar-transurethral resection of the prostate to surgically treat moderate-to-severe LUTS in men with prostate size of 30-80 mL.	Strong

5.3.1.2 Holmium laser resection of the prostate

With the advent of holmium laser enucleation of the prostate (section 5.3.2.3) and the fact that no relevant publications on holmium laser resection of the prostate (HoLRP) have been published since 2004, HoLRP of the prostate does not play a role in contemporary treatment algorithms.

5.3.1.3 Thulium:yttrium-aluminium-garnet laser vaporesection of the prostate

Mechanism of action: In the *Thulium:yttrium-aluminium-garnet laser* (Tm:YAG), a wavelength between 1,940 and 2,013 nm is emitted in continuous wave mode. The laser is primarily used in front-fire applications [335]. Different applications such as vaporesection (ThuVARP) have been published [336].

Efficacy: Several meta-analyses with pooled data from both RCTs, and non-RCTs have evaluated ThuVARP vs. M-TURP [337-339], and B-TURP [340-342]. The largest meta-analyses included nine RCTs and seven non-RCTs and reported no clinically relevant differences in efficacy (IPSS, QoL score and Q_{max}) between ThuVARP and M-TURP or B-TURP at twelve months [341]. A multicentre, RCT with 410 men reported that ThuVARP and TURP are equivalent in terms of IPSS but not Q_{max}, with TURP deemed superior at twelve months follow-up [343]. The beneficial effect of TURP in terms of Q_{max} was strengthened in men aged < 70 years and in those diagnosed with LUTS rather than urinary retention. No differences in individual patient-reported urinary symptoms were seen between arms, with the exception of some evidence to indicate potential reduction in nocturia in the TURP arm. Data from one RCT with long-term follow-up showed no difference in efficacy and re-operation rates between ThuVARP and M-TURP (2.1% vs. 4.1%, respectively) [344]. A prospective multicentre study on ThuVARP, including 2,216 patients, showed durable post-operative improvement in IPSS, QoL, Q_{max}, and PVR for the entire eight years of follow-up [345].

Tolerability and safety: In a number of meta-analyses longer operation times, shorter catheterisation/ hospitalisation times and less blood loss without significant differences in transfusion rates or in any other short-term complication rates have been reported for ThuVARP compared to TURP [337-342]. A significantly higher transfusion rate was reported after M-TURP in two meta-analyses [339, 341]. However, overall RCT quality was relatively low with limited follow-up potentially accounting for under-reporting of late complications,

such as urethral stricture/BNC [341]. A multicentre RCT with 410 men, followed up for twelve months reported that ThuVARP and TURP show similar operation, catheterisation, and hospitalisation times between arms with no difference in the frequency or severity of surgical complications or in blood transfusions rate or haemoglobin change [343, 346]. Patients with urinary retention had similarly positive outcomes to those with LUTS [343, 346]. Data from three RCTs with mid- to long-term follow-up (eighteen to 48 months) showed no differences in late complication rates between ThuVARP and TURP [344, 347, 348].

Haemoglobin drop was significantly higher in the bridging group in a retrospectively analysed case series of 103 patients who underwent ThuVARP and received either low molecular weight heparin bridging or continued antiplatelet/anticoagulant therapy [349].

Practical considerations: As a limited number of RCTs with mid- to long-term follow-up support the efficacy of ThuVARP, there is a need for ongoing investigation of the technique.

Summary of evidence	LE
Laser vaporesection of the prostate using Tm:YAG laser (ThuVARP) has similar operation, catheterisation and hospitalisation times compared to TURP. ThuVARP and TURP are equivalent in terms of IPSS but not Q_{max}, with TURP deemed superior at twelve months follow-up. ThuVARP and TURP show similar short-term safety. Mid- to long-term results on efficacy and safety compared to TURP are very limited.	1b

Recommendation	Strength rating
Offer laser resection of the prostate using Tm:YAG laser (ThuVARP) as an alternative to transurethral resection of the prostate.	Weak

5.3.1.4 Transurethral incision of the prostate

Mechanism of action: Transurethral incision of the prostate (TUIP) involves incising the bladder outlet without relevant tissue removal. Transurethral incision of the prostate is conventionally performed with Collins knife using electrocautery; however, alternative energy sources such as holmium laser may be used [350]. The mainstay of this technique is in prostate sizes < 30 mL without a middle lobe.

Efficacy: An RCT comparing conventional TUIP vs. TUIP using holmium laser in prostates ≤ 30 mL with a follow-up of twelve months, found both procedures to be equally effective in relieving BOO with similarly low re-operation rates [350]. A meta-analysis of ten RCTs found similar LUTS improvements and lower but significant improvements in Q_{max} for TUIP [351]. In this meta-analysis, an upper limit of prostate size was reported as an entry criterion for eight studies with five < 30 mL and three < 60 mL. A meta-analysis of six trials showed that re-operation was more common after TUIP (18.4%) than after M-TURP (7.2%) [351].

Tolerability and safety: An RCT comparing conventional TUIP vs. TUIP using holmium laser reported both procedures to be safe with low complication rates; however, the operation time and retrograde ejaculation rate was significantly lower in the conventional TUIP arm [350]. No cases of TUR-syndrome have been recorded after TUIP. The risk of bleeding after TUIP is small [351].

Practical considerations: Transurethral incision of the prostate is an effective treatment for moderate-to-severe LUTS secondary to BPO. The choice between M-TURP and TUIP should be based primarily on prostate volume (< 30 mL TUIP) [351].

Summary of evidence	LE
Transurethral incision of the prostate shows similar efficacy and safety to M-TURP for treating moderate-to-severe LUTS secondary to BPO in men with prostates < 30 mL.	1a
No case of TUR-syndrome has been recorded, the risk of bleeding requiring transfusion is negligible and retrograde ejaculation rate is significantly lower after TUIP, but the re-operation rate is higher compared to M-TURP.	1a
The choice between TUIP and TURP should be based primarily on prostate volume (< 30 mL and 30-80 mL suitable for TUIP and TURP, respectively).	4

Recommendation	Strength rating
Offer transurethral incision of the prostate to surgically treat moderate-to-severe LUTS in men with prostate size < 30 mL, without a middle lobe.	Strong

5.3.2 ***Enucleation of the prostate***

5.3.2.1 *Open prostatectomy*

Mechanism of action: Open prostatectomy is the oldest surgical treatment for moderate-to-severe LUTS secondary to BPO. Obstructive adenomas are enucleated using the index finger, approaching from within the bladder (Freyer procedure) or through the anterior prostatic capsule (Millin procedure). It is used for substantially enlarged glands (> 80-100 mL).

Efficacy: Open prostatectomy reduces LUTS by 63-86% (12.5-23.3 IPSS points), improves QoL score by 60-87%, increases mean Q_{max} by 375% (+16.5-20.2 mL/s), and reduces PVR by 86-98%. Efficacy is maintained for up to six years [352-357]. Data from an Austrian nationwide study of 1,286 men submitted to OP showed that the endourological re-intervention rates after primary OP were 0.9%, 3.0%, 6.0%, and 8.8%, at three months, one year, five years, and eight years, respectively [9].

Two meta-analyses [358, 359] evaluated the overall efficacy of OP performed via a transvesical approach vs. two transurethral enucleation techniques for treating patients with large glands, namely bipolar transurethral enucleation of the prostate (B-TUEP) and holmium laser enucleation of the prostate (HoLEP). Five RCTs compared OP with B-TUEP [357, 360-363] and four RCTs compared OP with HoLEP [352, 353, 364, 365]. At three, six, twelve and 24-months follow-up there were no significant differences in Q_{max} [359]. Post-void residual, PSA, IPSS and QoL score showed no significant differences during twelve-months follow-up [359]. Open prostatectomy and HoLEP had similar improvements regarding Q_{max}, IPSS score and re-operation rates after five years in one RCT [352].

Tolerability and safety: Two meta-analyses evaluated the overall safety of OP performed via a transvesical approach vs. B-TUEP and HoLEP [358, 359]. Operation time did not differ significantly between OP and B-TUEP but was significantly shorter for OP compared to HoLEP. Catheterisation and hospitalisation time were significantly longer for OP, which was also associated with more blood transfusions. There were no significant differences regarding other complications. There was no significant difference in IIEF-5 at three, six, twelve and 24-months follow-up.

Open prostatectomy mortality has decreased significantly during the past two decades (< 0.25%) [356]. Data from a study of 1,286 men submitted to OP showed mortality rates of 0.2% at 30 days and 0.4% at 90 days [309]. The estimated transfusion rate was about 7-14% [352, 355, 356, 358] Long-term complications include transient UI (up to 10%), BNC and urethral stricture (about 6%) [352-354, 358, 366].

Practical considerations: Open prostatectomy is the most invasive surgical method, but it is an effective and durable procedure for the treatment of LUTS/BPO. In the absence of an endourological armamentarium including a holmium laser or a bipolar system and with appropriate patient consent, OP is a reasonable surgical treatment of choice for men with prostates > 80 mL.

Summary of evidence	**LE**
Open prostatectomy is an effective and durable procedure for the treatment of LUTS/BPO, but it is the most invasive surgical method.	1b
Open prostatectomy shows similar short- and mid-term efficacy to B-TUEP and HoLEP for treating moderate-to-severe LUTS secondary to BPO in patients with large prostates.	1a
Open prostatectomy has a less favourable peri-operative safety profile compared to B-TUEP and HoLEP.	1a
The long-term functional results of OP are comparable to HoLEP.	1b

Recommendation	**Strength rating**
Offer open prostatectomy in the absence of bipolar transurethral enucleation of the prostate and holmium laser enucleation of the prostate to treat moderate-to-severe LUTS in men with prostate size > 80 mL.	Strong

5.3.2.2 *Bipolar transurethral enucleation of the prostate*

Mechanism of action: Following the principles of bipolar technology (section 5.3.1.1), the obstructive adenoma is enucleated endoscopically by the transurethral approach. Currently, two technologies exist, namely plasmakinetic (PK) enucleation of the prostate (PKEP) and bipolar plasma enucleation of the prostate (BPEP) [363, 367, 368]. Bipolar transurethral enucleation of the prostate is followed by either morcellation [363, 369] or resection [367, 370-374] of the enucleated adenoma.

Efficacy: Two meta-analyses, reported similar efficacy at twelve months in terms of IPSS, QoL score and Q_{max} for B-TUEP (PKEP or BPEP) vs. B-TURP [375, 376]. Another meta-analysis evaluating B-TUEP vs. B-TURP, reported similar efficacy at 36 months in terms of IPSS, and Q_{max} [325]. One RCT evaluating PKEP vs. M-TURP reported a significant improvement in IPSS, QoL score, and Q_{max}, with urodynamically proven de-obstruction favouring PKEP at 36-months follow-up [371]. One RCT evaluating PKEP vs. B-TURP in patients with prostate volume > 80 mL reported no clinically relevant differences in IPSS, QoL score, and Q_{max}, at six months follow up [377]. Another RCT evaluating BPEP vs. B-TURP in patients with prostate volume > 80 mL reported not clinically relevant differences in IPSS, QoL score, Q_{max} and PVR at 24-months follow-up [378]. Two RCTs evaluated the mid-term efficacy of PKEP vs. B-TURP at 36 months [372, 373] and one RCT evaluated long-term efficacy at 60 months [374]. Efficacy was significantly better for PKEP in patients with large prostates at 36, 48 and 60 months [372, 374]. Comparative data on efficacy for B-TUEP vs. OP and the various forms of laser enucleation are presented in section 5.3.2.1 – 5.3.2.5, respectively.

Tolerability and safety: Two meta-analyses evaluating B-TUEP vs. B-TURP reported similar operation, catheterisation and hospitalisation times; lower acute urine retention rates; significantly reduced haemoglobin drop and blood transfusion rates; no difference in ED; and no difference in all other reported complication rates including urethral stricture/BNC rates for B-TUEP at 24-months follow-up [375, 376]. [378]. A meta-analysis evaluating PKEP vs. TURP reported that mid-term IIEF-5 scores were comparable [379]. Another meta-analysis reported less bleeding with B-TUEP compared to M-TURP but similar UI rates and AUR after catheter removal [325]. An RCT evaluating PKEP vs. M-TURP in patients with prostate volume < 80 mL and 36-month follow-up reported that PKEP is superior to M-TURP in terms of catheterisation, and hospitalisation time [371]. No significant differences between the arms were reported in operation time, blood transfusion rates, sexual function, or any other reported complications (TUR-syndrome, clot retention, incontinence, retrograde ejaculation, urethral structures/BNC) [371]. One RCT evaluating PKEP vs. B-TURP in patients' prostate volume > 80 mL and six months follow-up reported that PKEP is superior to B-TURP in terms of operation, catheterisation and hospitalisation time [377]. Significant differences were reported in blood transfusion, BNC and retrograde ejaculation rates favouring PKEP, but no differences in urethral stricture and ED rates were reported [377]. Another RCT evaluating BPEP vs. B-TURP in patients with prostate volume > 80 mL reported that BPEP had longer operative time but shorter catheterisation, hospitalisation time with no differences in blood transfusion, urethral stricture and UI rates at 24-months follow-up [378]. No difference in urethral stricture/BNC rates was reported at 60 months follow-up [374]. Comparative data on efficacy for B-TUEP vs. OP and the various forms of laser enucleation are presented in section 5.3.2.1 – 5.3.2.5, respectively.

Summary of evidence	**LE**
Bipolar transurethral PKEP shows favourable mid- to long-term efficacy compared to TURP.	1b
Bipolar transurethral PKEP has a favourable peri-operative safety profile and demonstrates similar mid- to long-term safety compared to TURP.	1b

Recommendation	**Strength rating**
Offer bipolar transurethral (plasmakinetic) enucleation of the prostate to men with moderate-to-severe LUTS as an alternative to transurethral resection of the prostate.	Weak

5.3.2.3 Holmium laser enucleation of the prostate

Mechanism of action: The holmium:yttrium-aluminium garnet (Ho:YAG) laser (wavelength 2,140 nm) is a pulsed solid-state laser that is absorbed by water and water-containing tissues. Tissue coagulation and necrosis are limited to 3-4 mm, which is enough to obtain adequate haemostasis [380].

Efficacy: An initial meta-analysis reported no significant differences in short-term efficacy (Q_{max}) and re-intervention rates (4.3% vs. 8.8%) between HoLEP and M-TURP [381]; however, subsequent meta-analyses reported favourable short-term efficacy (Q_{max} and IPSS) for HoLEP [305, 338, 375, 382]. Another meta-analysis reported similar efficacy at 24-months in terms of IPSS, and Q_{max} [325]. Three meta-analyses evaluating HoLEP vs. B-TURP showed no significant differences in short-term efficacy (IPSS, QoL score and Q_{max}) [325, 375, 383]. One RCT comparing HoLEP with B-TURP in patients with prostate volume < 80 mL reported no significant difference in IPSS, QoL score and Q_{max} at 24-months [384]. One RCT comparing HoLEP with M-TURP in a small number of patients with mean prostate volume < 80 mL and a seven year follow-up found that the functional long-term results were comparable [385]. Another RCT comparing HoLEP with B-TURP in patients with prostate volume > 80 mL reported no significant difference in IPSS, QoL score and Q_{max} at 36 months, however, the overall re-treatment rate was significantly lower following HoLEP with less patients restarting α-blockers and less re-operations [386]. Comparative efficacy data for HoLEP vs. OP is presented in

section 5.3.2.1. One RCT evaluating HoLEP vs. PKEP in patients with mean prostate volume < 80 mL reported similar improvements in IPSS and Q_{max} at twelve months follow-up [369]. An RCT comparing HoLEP vs. bipolar transurethral enucleation reported no significant difference in IPSS, QoL score, PVR, and Q_{max} at one, three-, and twelve-months follow-up [387].

Tolerability and safety: Several meta-analyses found that HoLEP has longer operation times, shorter catheterisation and hospitalisation times, reduced blood loss, fewer blood transfusions but no significant differences in urethral strictures (2.6% vs. 4.4%) and stress urinary incontinence (SUI) (1.5% vs. 1.5%) rates compared to M-TURP [338, 375, 381, 382, 388]. Another meta-analysis reported that HoLEP has shorter catheterisation times, fewer blood transfusions, urethral strictures and UTIs but no significant differences in clot retention rates and AUR after catheter removal compared to M-TURP [325]. Three meta-analyses evaluated HoLEP vs. B-TURP [375, 383, 389]. One, reported longer operation times for HoLEP, but no significant differences in hospitalisation time or complication rates [375] whilst another reported no significant differences in operation and catheterisation times or short-term complication rates [383]. Data from a large national database on peri-operative outcomes of 2,869 laser enucleation of the prostate and 37,577 TURP procedures supports that laser enucleation of the prostate is associated with longer operation times, shorter hospitalisation times, similar complication rates (including transfusions, and re-operations), but lower rates of infectious complications [390]. A SR reported that HoLEP has lower AUR rates after catheter removal but similar haemoglobin drop, UTI, urethral stricture, and UI rates [325]. An RCT comparing HoLEP with B-TURP in patients with prostate volume < 80 mL reported longer operation time, shorter catheterisation and hospitalisation times and a lower risk for haemorrhage for HoLEP with no significant differences in blood transfusion rates or other complication rates at 24 months [384]. Another RCT comparing HoLEP with B-TURP in patients with prostate volume > 80 mL reported shorter operation, catheterisation and hospitalisation times and lower blood transfusion rates for HoLEP but no differences in complication rates including UI and IIEF-5 score at 36 months [386]. Comparative data on safety of HoLEP vs. OP are presented in section 5.3.2.1. One RCT evaluating HoLEP vs. PKEP in patients with mean prostate volume < 80 mL reported significantly shorter operation times for HoLEP, but similar catheterisation and hospitalisation times and complication rates at twelve months follow-up [369]. An RCT comparing HoLEP vs. bipolar B-TUEP demonstrated shorter operation and hospitalisation times and earlier catheter removal for HoLEP [387].

An RCT of pulse modulation in HoLEP (Virtual basket) demonstrated significantly less haemoglobin drop and reduced operation times when compared to conventional HoLEP [391].

Holmium laser enucleation of the prostate has been safely performed in patients using anticoagulant and/or antiplatelet medications [392, 393]. However, current limitations include: a lack of RCTs; limited data on short- and mid-term complications and bridging therapy; data presentation does not allow for separate interpretation of either antiplatelet and anticoagulant therapy.

A meta-analysis of seven RCTs evaluating HoLEP vs. TURP reported that short- and mid-term IIEF-5 scores were comparable, whilst long-term scores were significantly better for HoLEP [394]. Two other meta-analyses detected no difference in mid-term retrograde ejaculation rates [395].

The impact on erectile function and retrograde ejaculation is comparable between HoLEP and TURP [396, 397]. Erectile function did not decrease from baseline in either group; three quarters of sexually active patients had retrograde ejaculation after HoLEP. Data have shown that ejaculation and orgasm perception are the two most impacted domains after HoLEP [398]. Attempts to maintain ejaculatory function with HoLEP have been reported to be successful in up to 46.2% of patients [399].

An RCT comparing HoLEP vs. B-TUEP, reported shorter operation and hospitalisation times and earlier catheter removal for HoLEP [387].

Practical considerations: The experience of the surgeon is the most important factor affecting the overall occurrence of complications in HoLEP [400, 401]. Mentorship programmes are advised to improve surgical performance from both an institutional and personal learning curve perspective [402-404].

Summary of evidence	**LE**
Laser enucleation of the prostate using Ho:YAG laser (HoLEP) demonstrates similar mid- to long-term efficacy when compared to TURP.	1b
Laser enucleation of the prostate using Ho:YAG laser (HoLEP) demonstrates similar short-term safety when compared to TURP.	1a
Laser enucleation of the prostate using Ho:YAG laser (HoLEP) demonstrates longer operation times, but a more favourable peri-operative profile when compared to TURP.	1a

Recommendation	Strength rating
Offer laser enucleation of the prostate using Ho:YAG laser (HoLEP) to men with moderate-to-severe LUTS as an alternative to transurethral resection of the prostate or open prostatectomy.	Strong

5.3.2.4 Thulium:yttrium-aluminium-garnet laser enucleation of the prostate

Mechanism of action: The Tm:YAG laser has been described in section 5.3.1.3. Enucleation using the Tm:YAG laser includes thulium vapoenucleation of the prostate (ThuVEP) and thulium Laser enucleation of the prostate (ThuLEP) (blunt enucleation).

Efficacy: Two meta-analyses evaluating ThuLEP vs. M-TURP and B-TURP reported no clinically relevant differences in short-term efficacy (Q_{max}, IPSS and QoL score) [325, 375]. An RCT with five years follow-up comparing ThuLEP with B-TURP found no difference between the two procedures for Q_{max}, IPSS, PVR, and QoL [405]. A meta-analysis [406] evaluating ThuLEP vs. HoLEP showed no clinically relevant differences in IPSS, QoL score and Q_{max} at twelve months in accordance with one RCT showing similar results at eighteen months [407]. Furthermore, ThuLEP and PKEP were compared in one RCT with twelve months follow-up with no difference with regard to efficacy [408]. There are mainly prospective case studies on ThuVEP showing a significant improvement in IPSS, Q_{max}, and PVR after treatment [409-412].

Tolerability and safety: : Two meta-analyses evaluating ThuLEP vs. M-TURP and B-TURP reported a longer operation time and shorter catheterisation time for ThuLEP compared to M-TURP and a shorter hospitalisation time for ThuLEP compared to B-TURP [325, 375]. Lower blood transfusion rates compared to M-TURP, lower clot retention rates compared to B-TURP, and no difference in the other complication rates were also reported for ThuLEP [325, 375]. One meta-analysis [413] evaluating ThuLEP vs. HoLEP showed a significant difference in enucleation time favouring ThuLEP, but no significant differences in operation, catheterisation and hospitalisation times, and short-term complication rates. One RCT showed no urethral and bladder neck strictures at eighteen months after ThuLEP and HoLEP, respectively [407]. ThuLEP and PKEP were compared in one RCT with twelve months follow-up [408]. No significant difference in complication rates was detected, but haemoglobin level decrease and catheterisation time was significantly lower for ThuLEP. An RCT comparing ThuLEP with B-TURP reported a significant difference in IIEF-5 score favouring ThuLEP at twelve months [414].

In comparative studies ThuVEP shows high intra-operative safety [415], also in case series of patients with large prostates [409] and anticoagulation or bleeding disorders [410, 411]. A study focusing on post-operative complications after ThuVEP reported adverse events in 31% of cases, with 6.6% complications greater then Clavien grade 2 [416]. One case control study on ThuVEP with 48 month follow-up reported long-term durability of voiding improvements and overall re-operation rates of 2.4% [411].

Practical considerations: ThuLEP seems to offer similar efficacy and safety when compared to TURP, bipolar enucleation and HoLEP; whereas, ThuVEP is not supported by RCTs. Based on the limited number of RCTs there is a need for ongoing investigation of these techniques.

Summary of evidence	LE
Enucleation of the prostate using the Tm:YAG laser demonstrates similar efficacy when compared to M-TURP/bipolar transurethral (plasmakinetic) enucleation, HoLEP and B-TURP in the short-, mid-, and long-term, respectively.	1b
Enucleation of the prostate using the Tm:YAG laser (ThuLEP) demonstrates similar safety compared to TURP/bipolar transurethral (plasmakinetic) enucleation, and HoLEP in the short- and mid-term, respectively.	1b
Vapoenucleation of the prostate using a Tm:YAG laser (ThuVEP) seems to be safe in patients with large prostates and those receiving anticoagulant or antiplatelet therapy.	2b

Recommendations	Strength rating
Offer enucleation of the prostate using the Tm:YAG laser (ThuLEP, ThuVEP) to men with moderate-to-severe LUTS as an alternative to transurethral resection of the prostate, holmium laser enucleation or bipolar transurethral (plasmakinetic) enucleation.	Weak
Offer Tm:YAG laser enucleation of the prostate to patients receiving anticoagulant or antiplatelet therapy.	Weak

5.3.2.5 Diode laser enucleation of the prostate

Mechanism of action: For prostate surgery, diode lasers with a wavelength of 940, 980, 1,318, and 1,470 nm (depending on the semiconductor used) are marketed for vaporisation and enucleation. Only a few have been evaluated in clinical trials [385].

Efficacy: One RCT comparing 1,318 nm diode laser enucleation of the prostate (DiLEP) with B-TURP in patients with mean prostate volume < 80 mL reported no significant differences in IPSS, QoL score, Q_{max} and PVR at six months follow-up [417]. Another RCT comparing 1,470 nm DiLEP with B-TURP in patients with mean prostate volume < 80 mL also reported no significant differences in IPSS, QoL score, Q_{max} and PVR at twelve months follow-up [418]. In addition, three RCTs comparing 980 nm DiLEP with PKEP in patients with mean prostate volume < 80 mL [419, 420] and > 80 mL [421] reported no significant differences in IPSS, QoL score, Q_{max} and PVR at twelve months follow-up. An RCT of DilEP (980 nm) vs. HoLEP detected no significant difference in Q_{max}, PVR, IPSS, and QoL within twelve months follow-up [422].

Tolerability and safety: One small RCT comparing 1,318 nm DiLEP with B-TURP in patients with mean prostate volume < 80 mL and six months follow-up reported a significantly longer operation time for DiLEP, but shorter catheterisation and hospitalisation times, as well as less blood loss (without differences in blood transfusion rates) [417]. No differences in complication rates were reported between the two arms [417]. Another RCT comparing 1,470 nm DiLEP with B-TURP in patients with prostate volume < 80 mL and twelve months follow-up reported significantly shorter operation, catheterisation, and hospitalisation times with less blood loss (without differences in blood transfusion rates) for DiLEP, with no differences in complication rates between the two arms [418]. Three RCTs comparing 980 nm DiLEP with PKEP in patients with prostate volume < 80 mL [419, 420] and > 80 mL [421] and twelve months follow-up reported conflicting peri-operative outcomes. All trials reported no differences in blood transfusion rates and complication rates [419-421]. An RCT of DiLEP (980 nm) vs. HoLEP with twelve months follow-up demonstrated no significant difference in peri-operative outcomes including operation and hospitalisation times [422].

Practical considerations: Diode laser enucleation seems to offer similar efficacy and safety when compared to either B-TURP or bipolar transurethral (plasmakinetic) enucleation. Based on the limited number of mainly low-quality RCTs, and controversial data on the retreatment rate, results for DiLEP should be evaluated in further higher quality RCTs.

Summary of evidence	**LE**
Laser enucleation of the prostate using the 1,318 nm or 1,470 laser showed comparable short-term efficacy and safety to B-TURP. Peri-operative parameters like blood loss, catheterisation time and hospital stay are in favour of diode enucleation.	1b
Laser enucleation of the prostate using the 980 nm laser showed comparable short-term efficacy and safety to bipolar transurethral (plasmakinetic) enucleation.	1b

Recommendation	**Strength rating**
Offer 120-W 980 nm, 1,318 nm or 1,470 nm diode laser enucleation of the prostate to men with moderate-to-severe LUTS as a comparable alternative to bipolar transurethral (plasmakinetic) enucleation or bipolar transurethral resection of the prostate.	Weak

5.3.2.6 Enucleation techniques under investigation

5.3.2.6.1 Minimal invasive simple prostatectomy

Mechanism of action: The term minimal invasive simple prostatectomy (MISP) includes laparoscopic simple prostatectomy (LSP) [423] and robot-assisted simple prostatectomy (RASP) [424]. Both LSP and RASP are performed using different personalised techniques, based on the transcapsular (Millin) or transvesical (Freyer) approach.

Efficacy: A SR and meta-analysis showed that in 27 observational studies including 764 patients mean increase in Q_{max} was 14.3 mL/s, and the mean improvement in IPSS was 17.2 [425]. There were no differences in improvements in Q_{max} and IPSS [425]. A meta-analysis comparing MISP vs. OP reported no significant differences with regard to functional and symptom parameters between the two techniques [426]. A multicentre RCT with median follow-up of 26 months did not demonstrate any significantly different functional or peri-operative results between LSP, RASP and HoLEP [427].

Tolerability and safety: A meta-analysis comping MISP vs. OP demonstrated shorter hospital stay, as well as blood loss and transfusion rates for MISP [426]. In comparative studies to OP, length of hospital stay, length of catheter use, and estimated blood loss were significantly lower in the MISP group, while the duration of surgery was longer. There were no differences in peri-operative complications between both procedures [425]. In a multicentre RCT comparing LSP, RASP and HoLEP LSP demonstrated significantly longer catheterisation times than RASP and HoLEP, whilst RASP and LSP showed longer hospitalisation times and lower rates of *de novo* bladder storage symptoms [427]. In a comparative analysis of robotic vs. OP for large-volume prostates, a propensity score-matched analysis was performed with five covariates. Robotic compared with OP demonstrated a significant shorter average length of hospital stay, but longer mean operative time. The robotic approach was associated with a lower estimated blood loss. Improvements in maximal flow rate, IPSS, QoL, PVR and post-operative PSA levels were similar for both groups. There was no difference in complications between the groups [428].

Practical considerations: Currently, most studies on MISP are of a retrospective nature. High-quality studies are needed to compare efficacy, safety, and hospitalisation times, learning curve and costs of MISP and both OP and endoscopic methods.

Summary of evidence	**LE**
Minimal invasive simple prostatectomy is feasible in men with prostate sizes > 80 mL needing surgical treatment; however, RCTs are needed.	2a

5.3.2.6.2 532 nm ('Greenlight') laser enucleation of the prostate

Two approaches for Potassium-Titanyl-Phosphate (KTP) and the lithium triborate (LBO) laser-based enucleation technique exist [429]. GreenLEP is an anatomical enucleation technique following the principle of blunt dissection of the adenoma with the sheath and laser energy for incision as described for ThuLEP [430]. A variation is the *in-situ* vaporisation of apically enucleated tissue, also referred to as anatomic vaporisation-incision technique [430, 431]. To date, no RCTs evaluating enucleation using the KTP/LBO laser have been carried out [432].

*5.3.3 **Vaporisation of the prostate***

5.3.3.1 Bipolar transurethral vaporisation of the prostate

Mechanism of action: Bipolar transurethral vaporisation of the prostate (B-TUVP) utilises a bipolar electrode and a high-frequency generator to create plasma field (thin layer of highly ionized particles) to vaporise prostatic tissue [433]. Bipolar transurethral vaporisation of the prostate displays thinner (< 2 mm) coagulation zones [434], compared to monopolar TUVP (up to 10 mm) [435], potentially resulting in fewer irritative side-effects and SUI [434, 436, 437].

Efficacy: Bipolar-TUVP has been compared to TURP in thirteen RCTs, including a total of 1,244 men with a prostate size of < 80 mL [319, 438-449]. Early RCTs evaluated the PK B-TUVP system [438-442]; however, during the last decade, only the "plasma" B-TUVP system with the "mushroom- or button-like" electrode (Olympus, Medical) has been evaluated [319, 443-449]. Results have been pooled in three meta-analyses [305, 450, 451], and a narrative synthesis has been produced in two SRs [305, 452].

Follow-up in most RCTs is twelve months [438-441, 443-445, 447, 449] with the longest being 36 months in a small RCT (n = 40) and eighteen months in a subsequent RCT (n = 340); evaluating PK [442] and plasma B-TUVP [319], respectively. Pooled results from meta-analyses concluded that no significant differences exist in short-term efficacy (IPSS, QoL score, Q_{max} and PVR) between PK B-TUVP and TURP [305, 325, 451] and this was confirmed in a separate SR of seven RCTs [452]. However, the promising initial efficacy profile of the former may be compromised by inferior clinical outcomes (IPSS and Q_{max}) at mid-term. Higher quality RCTs with longer follow-up are necessary to draw definite conclusions on mid and long-term outcomes [305, 442].

Tolerability and safety: Early pooled results concluded that no statistically significant differences exist for intra-operative and short-term complications between PK B-TUVP and TURP, but peri-operative complications are significantly fewer after B-TUVP [305]. However, the results of a statistical analysis comparing pooled specific complication rates were not directly reported in this meta-analysis [305]. Mid-term complications (urethral stricture, ED, and retrograde ejaculation) are similar [442], but larger RCTs with longer follow-up are necessary to draw definite conclusions [305, 442]. A SR of seven RCTs comparing PK and plasma B-TUVP with TURP concluded that most RCTs shorter catheterisation (42.5 vs. 77.5 hours) and hospitalisation times (3.1 vs. 4.4 days) with B-TUVP [452], but another SR concluded that heterogeneity of RCTs, and methodological

limitations do not permit firm conclusions [305]. A meta-analysis reported that B-TUVP has shorter and similar catheterisation time compared to M-TURP and B-TURP, respectively; significantly fewer clot retentions/blood transfusions compared to M-TURP but not B-TURP; and no difference in other complication rates compared to either TURP technique [325]. A meta-analysis of six RCTs specifically evaluating plasma B-TUVP vs. TURP, concluded that no significant differences exist between the techniques in overall complication and transfusion rates [451]. However, a statistically significant difference was detected in major complication rates (Clavien 3, 4), including urethral stricture, severe bleeding necessitating re-operation and UI, and in the duration of catheterisation, favouring plasma B-TUVP.

Practical considerations: Bipolar-TUVP and PK TUVP have similar short-term efficacy to TURP, but with a favourable short-term safety profile. However, heterogeneity of RCTs, non-standardised techniques and methodological limitations do not permit firm conclusions, and multicentre, long-term RCTs s are needed.

Summary of evidence	**LE**
Bipolar-TUVP and TURP have similar short-term efficacy.	1a
Plasmakinetic B-TUVP has a favourable peri-operative profile, similar mid-term safety but inferior mid-term efficacy compared to TURP.	1a
Plasma B-TUVP has a lower short-term major morbidity rate compared to TURP.	1a

Recommendation	**Strength rating**
Offer bipolar transurethral vaporisation of the prostate as an alternative to transurethral resection of the prostate to surgically treat moderate-to-severe LUTS in men with a prostate volume of 30-80 mL.	Weak

5.3.3.2 532 nm ('Greenlight') laser vaporisation of the prostate

Mechanism of action: The KTP and LBO lasers have been described in section 5.3.2.6.2.

Efficacy: Meta-analyses of RCTs comparing photoselective vaporisation of the prostate (PVP) using the 80-W and 120-W lasers with TURP have reported no difference in Q_{max} and IPSS between 80-W or 120-W PVP and TURP [453, 454]. Another meta-analysis of four RCTs including 559 patients, on the 120-W laser, demonstrated no significant difference in functional and symptomatic parameters at 24-month follow-up when compared to TURP [455]. A meta-analysis of two RCTs reported similar efficacy of 120-W PVP, compared to M-TURP at 36-months follow-up [325].

The only available RCT for the 180-W laser reported non-inferiority to TURP in terms of IPSS, Q_{max}, PVR, prostate volume reduction, PSA decrease and QoL questionnaires. Efficacy outcomes were similar to TURP with stable results at 24-months follow-up [456].

One RCT comparing HoLEP to PVP, in patients with prostates > 60 mL, showed comparable symptom improvement, but significantly higher flow rates and lower PVR volume after HoLEP at short-term follow-up; in addition, PVP showed a 22% conversion rate to TURP [457].

One RCT compared B-TUVP with PVP with the 180-W XPS Laser. Comparable improvement in IPSS and Q_{max} were reported at 24-months follow-up [458].

Tolerability and safety: A meta-analysis of RCTs comparing the 80-W and 120-W lasers with TURP showed shorter catheterisation time (mean difference 32 hours) and length of hospital stay (mean difference 1.85 days) after PVP [305]. Blood transfusions and clot retention were less with PVP. No difference was noted in post-operative urinary retention, UTI, meatal stenosis, urethral stricture, or bladder neck stenosis [305]. A meta-analysis including trials with the 120-W laser likewise reported lower transfusion rates, catheterisation time and duration of hospital stay compared to TURP. Re-operation rates and operation time were in favour of TURP. No significant differences were demonstrated for treatment for urethral stricture, BNC, incidence of incontinence and UTI [455]. A meta-analysis confirmed that PVP was superior to both M-TURP/B-TURP with regard to catheterisation and to M-TURP but not to B-TURP with regard to transfusion rate and clot retention [325]. In an RCT comparing the 120-W HPS laser with TURP, with a follow-up of 36-months, the re-operation rate was significantly higher after PVP (11% vs. 1.8%) [459].

180-W Greenlight laser prostatectomy is non-inferior to TURP in terms of peri-operative complications. Re-operation free survival during a 24-month follow-up was comparable between the TURP-arm and the 180-W XPS laser-arm [456].

Based mostly on case series, the 80-,120- and 180-W Greenlight laser appears to be safe in high-risk patients undergoing anticoagulation treatment [460-463]; however, patients under anticoagulation therapy were either excluded from or represented a very small sample in currently available RCTs. In one

study, anticoagulated patients had significantly higher rates of bladder irrigation (17.2%) compared with those not taking anticoagulants (5.4%) [463]. In contrast, another retrospective study focusing on the 180-W LBO laser did not find any significant differences between patients receiving or not receiving anticoagulants [464]. A retrospective study of a mixed cohort of patients, treated with 80-W KTP PVP and 120-W LBO HPS, revealed that delayed gross haematuria was common in patients (33.8%) during an average follow-up of 33 months [465]. A retrospective review of a database of patients undergoing 180-W PVP, without interruption of anticoagulation therapy, had a 30.5% rate of peri-operative adverse events with a significant occurrence of high grade Clavien Dindo events [466].

Safety in patients with urinary retention, impaired detrusor contractility, elderly patients or prostates > 80 mL was shown in various prospective short-term non-randomised trials. No RCT including prostates > 100 mL has been reported; therefore, comparison of retreatment rates between prostate volumes of different sizes is not possible [467-469].

A meta-analysis of five RCTs comparing collectively all three "Greenlight" lasers with TURP detected no difference in retrograde ejaculation rates [395]. Additional studies have also reported no difference between OP/TURP and Greenlight PVP for erectile function [470, 471]. However, IIEF-5 scores were significantly decreased at six-, twelve-, and 24- months in patients with pre-operative IIEF-5 greater than nineteen [472].

No significant difference with respect to peri- and post-operative complications was reported in an RCT comparing B-TUVP and PVP with the 180-W XPS Laser. Redo TURP for recurrent adenoma was required in 9.8% (B-TUVP) and 1.7% (PVP) of the patients during 24-months follow-up, respectively [458].

Practical considerations: The 180-W XPS represents the current standard of generators for PVP; however, the number and quality of supporting publications are low, especially for large glands (> 100 mL), with no long-term follow-up.

Summary of evidence	**LE**
Laser vaporisation of the prostate using the 80-W KTP and the 120-W LBO laser (PVP) demonstrated higher intra-operative safety with regard to haemostatic properties when compared to TURP. Peri-operative parameters such as catheterisation time and hospital stay are in favour of PVP, whereas operation time and risk of re-operation are in favour of TURP. Short-term results for the 80-W KTP laser and mid-term results for the 120-W LBO laser were comparable to TURP.	1a
Laser vaporisation of the prostate using the 180-W LBO laser (PVP) demonstrated higher intra-operative safety with regard to haemostatic properties when compared to TURP. Peri-operative parameters such as catheterisation time and hospital stay were in favour of PVP, whereas operation time was in favour of TURP. Short- to mid-term results are comparable to TURP.	1b
Laser vaporisation of the prostate using the 80-W KTP and 120-W LBO lasers seems to be safe for the treatment of patients receiving antiplatelet or anticoagulant therapy.	2
Laser vaporisation of the prostate using the 180-W LBO laser seems to be safe for the treatment of patients receiving antiplatelet or anticoagulant therapy; however, the level of evidence available is low.	3

Recommendations	**Strength rating**
Offer 80-W 532-nm Potassium-Titanyl-Phosphate (KTP) laser vaporisation of the prostate to men with moderate-to-severe LUTS with a prostate volume of 30-80 mL as an alternative to transurethral resection of the prostate (TURP).	Strong
Offer 120-W 532-nm Lithium Borat (LBO) laser vaporisation of the prostate to men with moderate-to-severe LUTS with a prostate volume of 30-80 mL as an alternative to TURP.	Strong
Offer 180-W 532-nm LBO laser vaporisation of the prostate to men with moderate-to-severe LUTS with a prostate volume of 30-80 mL as an alternative to TURP.	Strong
Offer laser vaporisation of the prostate using 80-W KTP, 120- or 180-W LBO lasers for the treatment of patients receiving antiplatelet or anticoagulant therapy with a prostate volume < 80 mL.	Weak

5.3.3.3 Vaporisation techniques under investigation

5.3.3.3.1 Diode laser vaporisation of the prostate

Mechanism of action: Diode lasers with a wavelength of 980 nm are marketed for prostate vaporisation; however, only a few have been evaluated in clinical trials [335].

Efficacy: Two RCTs for 120-W 980 nm diode laser vaporisation vs. M-TURP are available [473, 474]. The first RCT with 24-month follow-up reported similar efficacy (IPSS, Q_{max} and PVR) at one- and six -months. However, at twelve- and 24-months improvements in IPSS and Q_{max} were significantly in favour of TURP, and repeat

TURP was more frequent in the diode laser group [473]. The second RCT reported equivalent results for both interventions at three-month follow-up [474].

Tolerability and safety: A meta-analysis comparing diode laser vaporisation vs. M-TURP reported shorter catheterisation time and lower transfusion rates for diode laser vaporisation [325]. In an RCT reflecting on peri-operative and post-operative complications no significant differences were demonstrated for clot retention, AUR after catheter removal, UUI and UTI [473]. Moreover, for late complications no significant differences could be demonstrated for re-operation rate, urethral stricture, bladder neck sclerosis, de novo sexual dysfunction and mean time of dysuria [473]. Published studies on 980 nm diode laser vaporisation indicate high haemostatic potential, although anticoagulants or platelet aggregation inhibitors were taken in 24% and 52% of patients, respectively [475, 476]. In a number of studies, a high rate of post-operative dysuria was reported [473, 475-477].

Early publications on diode vaporisation reported high re-operation rates (8-33%) and persisting SUI (9.1%) [473, 475-477].

Practical considerations: Diode laser vaporisation leads to similar improvements in clinical and symptomatic parameters during short-term follow-up and provides good haemostatic properties. Based on the limited number of mainly low quality RCTs, and controversial data on the retreatment rate, results for diode laser vaporisation should be evaluated in further higher quality RCTs.

Summary of evidence	**LE**
Laser vaporisation of the prostate using the 120-W 980 nm diode laser demonstrated high intra-operative safety with regard to haemostatic properties when compared to TURP. Peri-operative parameters like catheterisation time and hospital stay were in favour of diode lasers. Evidence is limited by the number and quality of the available studies.	1b
In a number of studies, post-operative complications such as severe storage symptoms and persisting incontinence, occurred with laser vaporisation of the prostate using the 120-W 980 nm diode laser.	3
Laser vaporisation using the 120-W 980 nm diode laser seems to be safe with regard to haemostasis in patients receiving anticoagulant therapy.	3

*5.3.4 **Alternative ablative techniques***

5.3.4.1 Aquablation – image guided robotic waterjet ablation: AquaBeam

Mechanism of action: AquaBeam uses the principle of hydro-dissection to ablate prostatic parenchyma while sparing collagenous structures like blood vessels and the surgical capsule. A targeted high velocity saline stream ablates prostatic tissue without the generation of thermal energy under real-time transrectal ultrasound guidance. After completion of ablation haemostasis is performed with a Foley balloon catheter on light traction or diathermy or low-powered laser if necessary [478].

Efficacy: In a double-blind, multicentre, pivotal RCT, 181 patients with a prostate size of 30-80mL were randomised to TURP or Aquablation [479, 480]. Mean total operative time was similar for Aquablation and TURP (33 vs. 36 minutes), but resection time was significantly lower for Aquablation (4 vs. 27 minutes). At six months patients treated with Aquablation and TURP experienced large IPSS improvements (-16.9 and -15.1, respectively), satisfying the non-inferiority hypothesis. At one year follow-up, mean IPSS reduction was 15.1 with a mean reduction in IPSS score of 67% for both groups. No significant difference in improvement of IPSS, QoL, Q_{max} and reduction of PVR was reported between the groups [481].

Improvements in IPSS and Q_{max} were maintained after three years in both groups [482]. Mean IPSS improvements were 14.4 and 13.9 points in the Aquablation and TURP groups, respectively. Similarly, three-year improvements in Q_{max} were 11.6 and 8.2 mL/s [483]. Over three years, surgical retreatments were 4.3% and 1.5% respectively. Cohort studies reported similar, consistent results [484].

Results of AquaBeam in patients with large prostates (80-150mL) were evaluated in a cohort study of 101 men (WATER II) [479]. After twelve months, significant improvements were seen in IPSS (mean decrease of 17 points), Q_{max} (increase of 12.5 cc/sec) and PVR (a drop of 171 cc in those with PVR > 100 at baseline). No patient underwent a repeat procedure for BPH symptoms [485]. Improvement was maintained at two years, with a surgical retreatment rate of 2% in WATER II [486].

Another RCT comparing Aquablation with TURP performed urodynamic studies on 66 patients at six months follow-up and reported significant changes in $p_{det}Q_{max}$ (reductions of 35 and 34 cm H_20, respectively) and large improvements in BOO index in both groups [487].

Tolerability and safety: Results for the WATER trial have shown comparable hospital stay and catheterisation duration (1.4 and 1 day, respectively) [479]. One case of blood transfusion was reported after Aquabeam and none after TURP. In a SR of seven patient groups involving 446 patients treated by aquablation, although there was a significant haemoglobin drop (2.06 g/dL), it did not translate into increased transfusion rates. In WATER, fewer men in the Aquablation group had a persistent Clavien-Dindo grade 1 or 2 or higher adverse event compared to TURP (26% vs. 42%) at three months. Among sexually active men the rate of an ejaculation was lower in those treated with Aquablation compared to TURP (10% vs. 36%, respectively). There were no procedure-related adverse events after six months [481].

In patients with a prostate volume between 80-150 mL (WATERII trial), bleeding related events were observed in fourteen patients (13.9%) of which eight (7.9%) occurred prior to discharge and six (5.9%) occurred within one month of discharge. Blood transfusions were required in eight patients, return to the theatre for fulguration in three patients, and both transfusion and fulguration in two patients [488]. Maintenance of antegrade ejaculation was slightly lower in WATER II at 81% compared to 90% in the smaller prostates of WATER I [489]. In WATER II there was a 2% de novo incontinence rate at twelve months [490].

Practical considerations: During mid-term follow-up, aquablation provides non-inferior functional outcomes compared to TURP in patients with LUTS and a prostate volume between 30-80 mL. Longer term follow-up is necessary to assess the clinical value of aquablation.

Summary of evidence	**LE**
Aquablation appears to be as effective as TURP both subjectively and objectively; however, there are still some concerns about the best methods of achieving post-treatment haemostasis.	1b

Recommendations	**Strength rating**
Offer Aquablation* to patients with moderate-to-severe LUTS and a prostate volume of 30-80 mL as an alternative to transurethral resection of the prostate.	Weak
Inform patients about the risk of bleeding and the lack of long-term follow-up data.	Strong

** Aquablation remains under investigation*

5.3.4.2 Prostatic artery embolisation

Mechanism of action: Prostatic artery embolisation (PAE) can be performed as a day procedure under local anaesthesia with access through the femoral or radial arteries. Digital subtraction angiography displays arterial anatomy, and the appropriate prostatic arterial supply is selectively embolised to effect stasis in treated prostatic vessels. Different technical variations (including bead size) have been described for PAE, which needs specific training [491, 492].

Efficacy: Superior efficacy of PAE compared with a sham procedure was found in a six-month randomised, single-blind, sham-controlled trial in 80 patients with LUTS, refractory to medical treatment. The decrease in IPSS at six months was 5.03 +/- 8.13 in the sham group and 17.1 +/- 7.25 in the PAE group [493].

A SR and meta-analysis including RCTs and two non-RCTs comparative studies (n = 708 patients) showed that TURP achieved a significantly higher mean post-operative difference for IPSS and IPSS-QoL, 3.80 and 0.73 points, respectively compared to PAE [494]. All of the functional outcomes assessed were significantly superior after TURP: 3.62 mL/s for Q_{max}, 11.51 mL for prostate volume, 11.86 mL for PVR, and 1.02 ng/mL for PSA [494]. Another SR and meta-analysis including six studies with 598 patients showed that TURP resulted in significantly greater improvement in Q_{max}, prostate volume, and PSA compared to PAE [495]. However, there was no significant difference between PAE and TURP in IPSS improvement, IPSS QoL, IIEF and PVR [495]. Another SR and meta-analysis of ten RCTs (one vs. sham, five vs. TURP and four exploring variations in PAE technique) confirmed that PAE is non-inferior to TURP in improving patient reported outcome measures (PROMs), though TURP is superior to PAE for most objective outcomes [496].

According to a non-inferiority trial, 21% of patients who initially had PAE underwent TURP within two years [497].

In a single centre retrospective analysis of 75 PAE patients over a three-year period, PAE was shown to be a safe, effective, and durable treatment option for non-index patients with urinary retention (87% catheter free) or gross haematuria (resolved 87.5%) [498].

Tolerability and safety: Available RCTs, as well as SR and meta-analyses show conflicting results about the comparative rate of adverse events after PAE or TURP, depending on studies included, definition of adverse

events, and follow-up. In a SR of comparative studies PAE resulted in significantly more adverse events than TURP/OP (41.6% vs. 30.4%). The frequency of AUR after the procedures was significantly higher in the PAE group (9.4% vs. 2.0%) [499]. In another compilation of studies, PAE was associated with significantly fewer overall adverse events but similar rates of severe side effects, as well as and shorter hospitalisation times (mean difference = -1.94 days), but longer procedural times (mean difference = 51.43 min) [495].

Another SR and meta-analysis of four studies (506 patients) comparing PAE and TURP found no significant difference in the post-operative complication rate between TURP and PAE [500].

Concerning sexual adverse events, the mean differences in IIEF-5 score were not significantly different between TURP and PAE in a meta-analysis [495]. Another meta-analysis of two RCTs detected no difference in retrograde ejaculation rates [395]. Post-operative erectile function measured by IIEF-5 was in favour of PAE with mean difference in change of 2.56 points. In another updated meta-analysis PAE was consistently associated with lower sexual dysfunction than TURP (OR 0.24) [501].

Concerns still exist about non-target embolisation, reported in earlier studies [502]; however, more recent studies report less incidents [494, 503]. A SR of 22 studies reporting radiation exposure during PAE, with a twenty-fold range of exposures, estimated that the median risk for a 66-year-old patient of a cancer related death was 0.117%, equivalent to a reduced life expectancy of 5.4 days. Radiation exposure therefore should be part of the counselling for patients considered for PAE. These data suggest there is potential for significant radiation reduction in some centres using appropriate protocols [504].

Practical considerations: A multidisciplinary team approach of urologists and radiologists is mandatory and patient selection should be done by urologists and interventional radiologists. The investigation of patients with LUTS to indicate suitability for invasive techniques should be performed by urologists only. This technically demanding procedure should only be done by an interventional radiologist with specific mentored training and expertise in PAE [505]. There are data suggesting that larger prostates have a higher chance of a superior outcome with PAE in *post hoc* analysis of RCTs, but larger trials are required to clarify the most suitable patients for PAE [488, 506].

Further data with medium- and long-term follow-up are still required and comparison with other minimally invasive techniques would be valuable. However, current evidence of safety and efficacy of PAE appears adequate to support the use of this procedure for men with moderate-to-severe LUTS provided proper arrangements for consent and audit are in place; therefore, a recommendation has been given, but PAE remains under investigation.

Summary of evidence	**LE**
Prostatic artery embolisation (PAE) is less effective than TURP at improving symptoms and urodynamic parameters such as flow rate.	1a
Procedural time is longer for PAE compared to TURP, but blood loss, catheterisation and hospitalisation time are in favour of PAE.	1b

Recommendations	**Strength rating**
Offer prostatic artery embolisation (PAE)* to men with moderate-to-severe LUTS who wish to consider minimally invasive treatment options and accept less optimal outcomes compared with transurethral resection of the prostate.	Weak
Perform PAE only in units where the work up and follow-up is performed by urologists working collaboratively with trained interventional radiologists for the identification of PAE suitable patients.	Strong

** PAE remains under investigation*

5.3.4.3 Alternative ablative techniques under investigation

5.3.4.3.1 Convective water vapour energy (WAVE) ablation: The Rezum system

Mechanism of action: The Rezum system uses radiofrequency power to create thermal energy in the form of water vapour, which in turn deposits the stored thermal energy when the steam phase shifts to the liquid phase upon cell contact. The steam disperses through the tissue interstices and releases stored thermal energy onto prostatic tissue effecting cell necrosis. The procedure can be performed in an office-based setting. Usually, one to three injections are needed for each lateral lobe and one to two injections may be delivered into the median lobe (depending on the prostate size).

Efficacy: In a multicentre RCT, 197 men were enrolled and randomised in a 2:1 ratio to treatment with water vapour energy ablation or sham treatment [507]. At three months relief of symptoms, (measured by a change in IPSS and Q_{max}) were significantly improved and maintained after WAVE therapy compared to the sham arm, although only the active treatment arm was followed up to twelve months. No relevant impact was observed on PVR. Quality of life outcome was significantly improved with a meaningful treatment response of 52% at twelve months. Further validated objective outcome measures such as BPH impact index (BPHII), Overactive Bladder Questionnaire Short Form for OAB bother, and impact on QoL and ICS Male Item Short Form Survey for male incontinence demonstrated improvements of symptoms at three months follow-up with sustained efficacy throughout the study period of twelve months. The reported two-year results in the Rezum cohort arm of the same study and the recently reported four-year results confirmed durability of the positive clinical outcome after convective water vapour energy ablation [508, 509]. Surgical retreatment rate was 4.4% over four years [509]. A Cochrane review found no studies comparing convective radiofrequency water vapour thermal therapy to any other active treatment form, such as TURP [510].

Tolerability and safety: Safety profile was favourable with adverse events documented to be mild-to-moderate and resolving rapidly. Preservation of erectile and ejaculatory function after convective water vapour thermal therapy was demonstrated utilising validated outcome instruments such as IIEF and Male Sexual Health Questionnaire-Ejaculation Disorder Questionnaire [507].

Practical considerations: There are two SRs of the Rezum cohort studies. One concludes that Rezum provides improvement in BPH symptoms that exceeds established minimal clinically important difference thresholds, preserves sexual function, and is associated with low surgical retreatment rates over four years. Therefore, suggesting that it may be a valuable addition to the urological armamentarium to treat LUTS in men with BPH [511]. The other, a Cochrane review reported that the certainty of evidence ranged from moderate to very low, with study limitations and imprecision being the most common reasons for down-grading of the evidence [510]. Randomised controlled trials against a reference technique are needed to confirm the first promising clinical results and to evaluate mid- and long-term efficacy and safety of water vapour energy treatment.

5.3.5 ***Non-ablative techniques***

5.3.5.1 Prostatic urethral lift

Mechanism of action: Prostatic urethral lift (PUL) is a minimally invasive approach under local or general anaesthesia. Encroaching lateral lobes are compressed by small permanent suture-based implants delivered under cystoscopic guidance resulting in an opening of the prostatic urethra leaving a continuous anterior channel through the prostatic fossa.

Efficacy: Several reports have shown that PUL achieves a significant improvement in IPSS (-39% to -52%), Q_{max} (+32% to +59%) and QoL (-48% to -53%) [512-517]. In a meta-analysis of retrospective and prospective trials, pooled estimates showed an overall improvement following PUL, including IPSS, Q_{max}, and QoL [517]. A Cochrane review of the sham RCT and the RCT against TURP concluded that PUL appears less effective than TURP in improving urological symptoms (IPSS, Q_{max}) in both short- and long term, while QoL outcomes may be similar [518]. Prostatic urethral lift was evaluated vs. sham in a multicentre study with one [514] three [519] and five [520] years follow-up of the treated cohort. Improvements in IPSS, QoL, and Q_{max} were durable with improvement rates of 36%, 50%, and 44% at 60-month follow-up, respectively [520].

A retrospective observational study of 1,413 consecutive patients from North America and Australia split patients into those still voiding (Group A) and those in retention (Group B). The results from Group A were comparable to the results from the clinical trials and of the 165 patients in Group B 69% were catheter free after five days, 83% after one month and 89% by study end [521].

Tolerability and safety: The most common complications reported post-operatively included haematuria (16-63%), dysuria (25-58%), pelvic pain (5-17.9%), urgency (7.1-10%), transient incontinence (3.6-16%), and UTI (2.9-11%) [514, 517, 519, 520]. Most symptoms were mild-to-moderate in severity and resolved within two to four weeks after the procedure. In an RCT comparing PUL to TURP, surgical recovery was measured using a validated instrument. They found that recovery from PUL is more rapid and more extensive in the first three to six months [522]. A SR and meta-analysis found that sexual function with regard to erectile and ejaculatory function remained stable or improved slightly during the 24-month follow-up [496, 517, 518].

In an RCT comparing PUL to TURP, PUL resulted in superior quality of recovery and ejaculatory function preservation. Ejaculatory function and bother scores did not change significantly in either treatment arm [522].

A SR of surgical re-interventions of eleven studies (2,016 patients), among which TURP/laser (51%), repeat PUL (32.7%) and device explant (19.6%) were most common, revealed an annual rate of surgical

re-intervention of 6% per year (95% CI: 3.0-8.9) [523]. The re-treatment rate was 13.6% over five years in a multicentre study comparing PUL vs. sham [520].

Practical considerations: There are only limited data on treating patients with an obstructed/protruding middle lobe [524]. The effectiveness in large prostate glands has not been shown yet. Long-term studies are needed to evaluate the duration of the effect in comparison to other techniques.

Summary of evidence	LE
Prostatic urethral lift improves IPSS, Q_{max} and QoL; these improvements are inferior to TURP at 24-months.	1b
Prostatic urethral lift has a low incidence of sexual side effects.	1b
Patients should be informed that long-term effects, including the risk of retreatment, have not been evaluated.	4

Recommendation	Strength rating
Offer Prostatic urethral lift (Urolift®) to men with LUTS interested in preserving ejaculatory function, with prostates < 70 mL and no middle lobe.	Strong

5.3.5.2 Intra-prostatic injections

Mechanism of action: Various substances have been injected directly into the prostate in order to improve LUTS including Botulinum toxin-A (BoNT-A), fexapotide triflutate (NX-1207) and PRX302. The primary mechanism of action of BoNT-A is through the inhibition of neurotransmitter release from cholinergic neurons [525]. The mechanisms of action for the injectables NX-1207 and PRX302 are not completely understood, but experimental data suggest apoptosis-induced atrophy of the prostate with both drugs [525].

Efficacy: A SR and meta-analysis showed no differences in efficacy of BoNT-A compared with placebo and concluded that there is no evidence of clinical benefit in medical practice [526]. The positive results from Phase II-studies have not been confirmed in Phase III-trials for PRX302 [527, 528]. NX-1207 was evaluated in two multicentre placebo controlled double-blind randomised parallel group trials including a total of 995 patients with a mean follow-up of 3.6 years, IPSS change from baseline was significantly higher and AUR rate was significantly reduced in the treatment arm. The authors concluded that NX-1207 is an effective transrectal injectable for long-term treatment for LUTS and that treated patients have reduced need for further intervention [529].

Tolerability and Safety: A SR and meta-analysis showed low incidence rates of procedure-related adverse events [526]. Two multicentre placebo controlled double-blind randomised parallel group trials with long-term follow-up evaluating NX-1207 detected no significant safety differences between the study arms [529].

Practical considerations: Positive results for PRX302 from Phase II-studies have not been confirmed in Phase III-trials yet. Nevertheless, an RCT evaluating transperineal intraprostatic BoNT-A injection vs. TURP concluded that IPSS significantly decreased in all patients, with a non-significant difference between the arms and that the BoNT-A injection significantly maintained erectile function compared to TURP at twelve months [530]. More high-quality evidence against reference techniques is needed.

Summary of evidence	LE
Results from clinical trials have shown no clinical benefits for BoNT-A compared to placebo for the management of LUTS due to BPO.	1a
Results from clinical trials have shown clinical benefits for NX-1207 compared to placebo for the management of LUTS due to BPO.	1b

Recommendation	Strength rating
Do not offer intraprostatic Botulinum toxin-A injection treatment to patients with male LUTS.	Strong

5.3.5.3 Non-ablative techniques under investigation

5.3.5.3.1 (i)TIND

Mechanism of action: The iTIND is a nitinol device composed of three elongated struts and an anchoring leaflet. Under direct visualisation iTIND is deployed inside the prostate in expanded configuration. The intended

mode of action is to compress obstructive tissue by the expanded device, thereby exerting radial force leading to ischaemic necrosis resulting in a Turner Warwick like incision. The iTIND device is left in position for five days and removed in an outpatient setting by standard urethroscopy.

Efficacy: A single-arm, prospective study of 32 patients with a three-year follow-up was conducted to evaluate feasibility and safety of the procedure [531]. The change from baseline in IPSS, QoL and Q_{max} was significant at every follow-up [532]. In a multicenter RCT, 175 men were randomised 2:1 between iTIND and sham procedures. Patients were assessed at baseline, 45 days, three, and twelve months postoperatively. A total of 78.6% of patients in the iTIND arm showed a reduction of ≥ 3 points in IPSS, vs. 60% of patients in the control arm at three months. At twelve months follow-up, the iTIND group reported a mean decrease of 9.25 in IPSS, of 1.9-point in QoL and a 3.52mL/s increase in Q_{max} compared to baseline [533]. In a prospective multicentre study, 81 patients were enrolled and treated with a second generation iTIND device. At twelve-month follow-up, mean IPSS decreased from 22.5 to 8.8 and Q_{max} at one month increased from 7.3 to 14.7 ml/s at twelve months [534].

Tolerability and safety: The device were reported as well tolerated by all patients. Four early complications (12.5%) were recorded, including one case of urinary retention (3.1%), one case of transient incontinence due to device displacement (3.1%), and two cases of infection (6.2%). No further complications were recorded during the 36-month follow-up period [532]. In the RCT against sham study adverse events were typically mild and transient, most were Clavien-Dindo grade 1 or 2 with 38.1% in the iTIND arm and 17.5% in the control arm [533]. No new ejaculatory or erectile dysfunction has been reported [533, 534].

In a prospective multicentre study, 81 patients were enrolled and treated with a second generation iTIND device. During the twelve-month period, two patients required medical therapy, two patients required TURP, and ten patients were lost to follow-up [534].

Practical considerations: Randomised controlled trials comparing iTIND to a reference technique are ongoing.

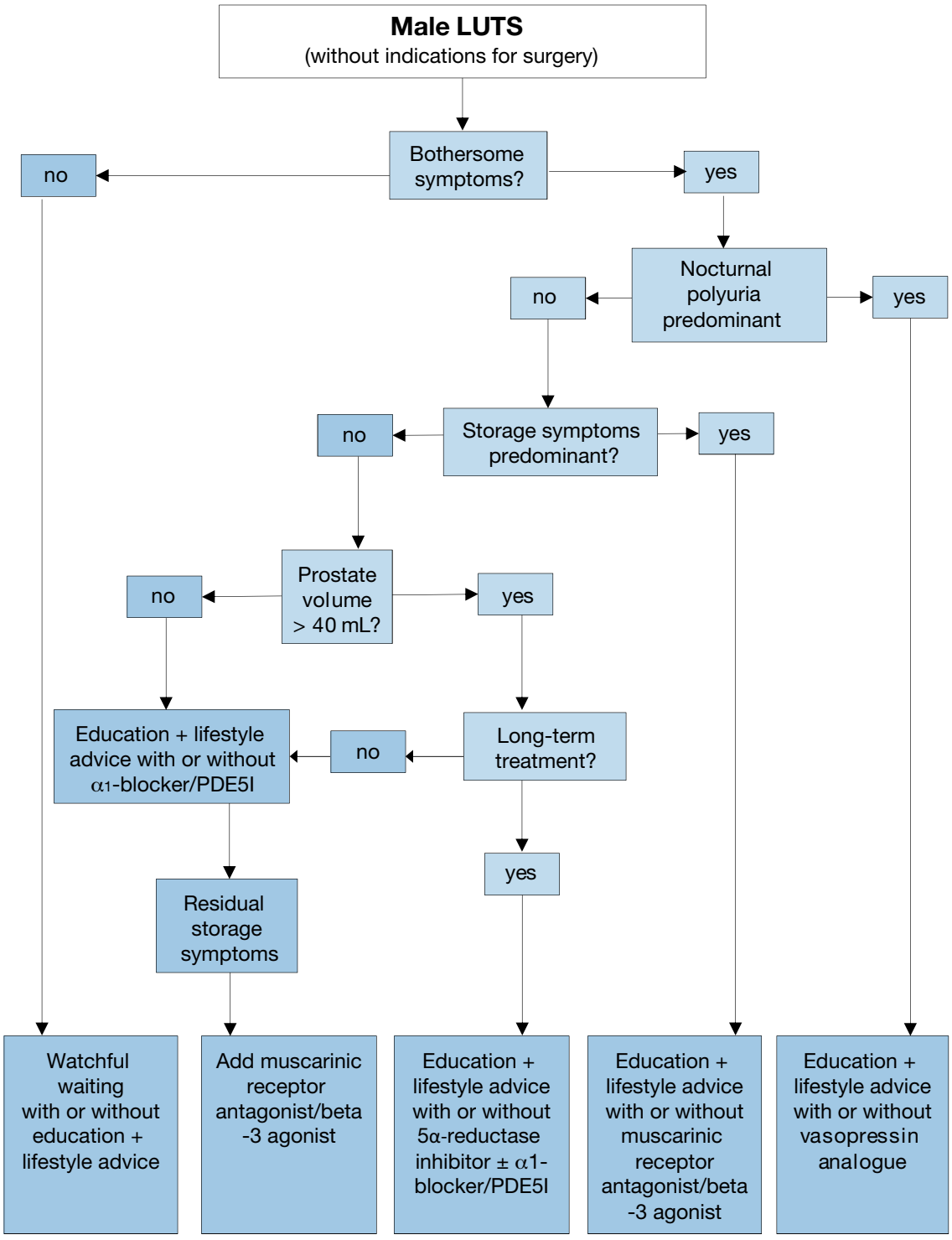
5.4 Patient selection

The choice of treatment depends on the assessed findings of patient evaluation, ability of the treatment to change the findings, treatment preferences of the individual patient, and the expectations to be met in terms of speed of onset, efficacy, side effects, QoL, and disease progression.

Behavioural modifications, with or without medical treatments, are usually the first choice of therapy. Figure 3 provides a flow chart illustrating treatment choice according to evidence-based medicine and patient profiles. Surgical treatment is usually required when patients have experienced recurrent or refractory urinary retention, overflow incontinence, recurrent UTIs, bladder stones or diverticula, treatment-resistant macroscopic haematuria due to BPH/BPE, or dilatation of the upper urinary tract due to BPO, with or without renal insufficiency (absolute operation indications, need for surgery).

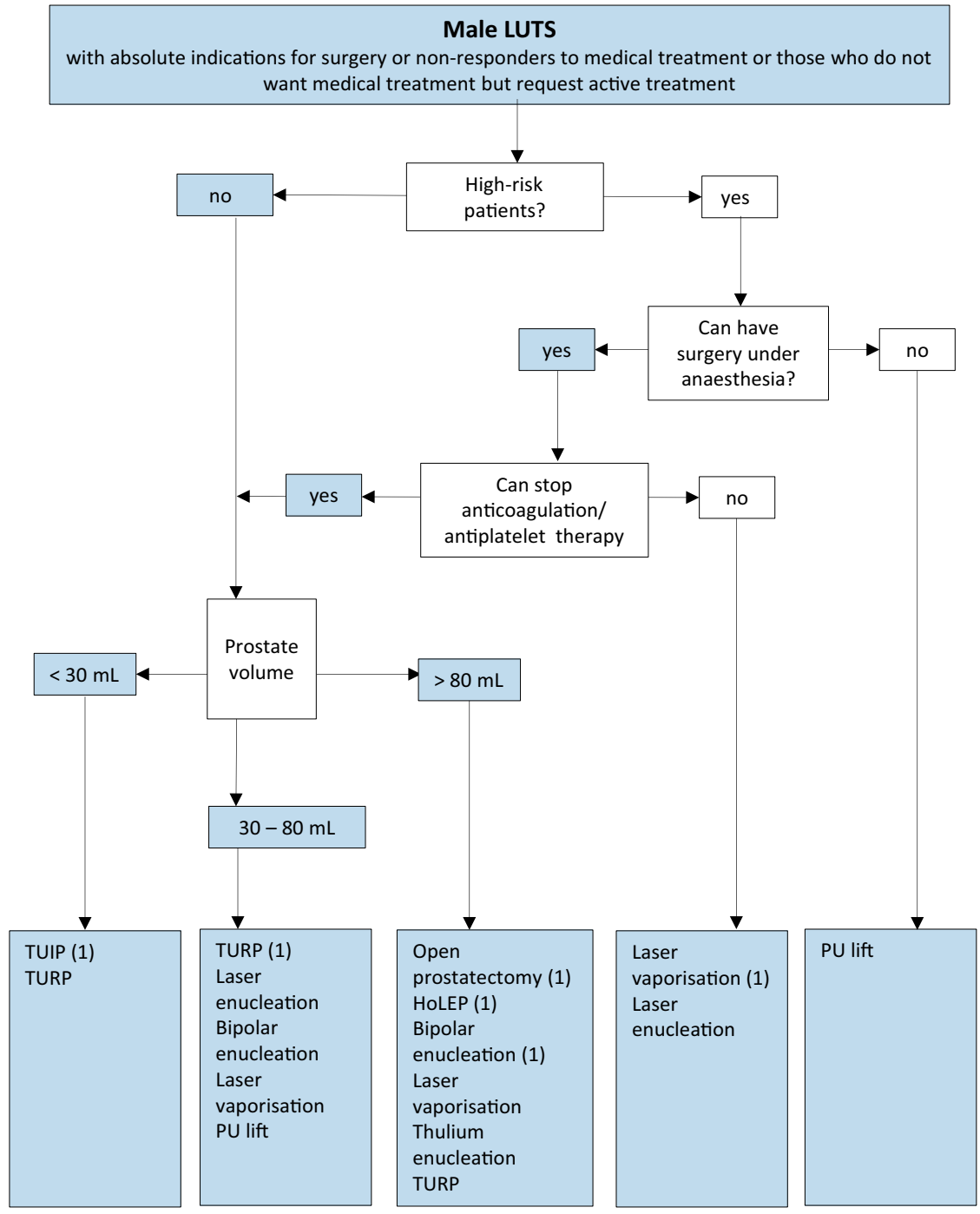
Additionally, surgery is usually needed when patients have not obtained adequate relief from LUTS or PVR using conservative or medical treatments (relative operation indications). The choice of surgical technique depends on prostate size, co-morbidities of the patient, ability to have anaesthesia, patients' preferences, willingness to accept surgery-associated specific side-effects, availability of the surgical armamentarium, and experience of the surgeon with these surgical techniques. An algorithm for surgical approaches according to evidence-based medicine and the patient's profile is provided in Figure 4.

Figure 3: Treatment algorithm of male LUTS using medical and/or conservative treatment options. Treatment decisions depend on results assessed during initial evaluation. Note that patients' preferences may result in different treatment decisions.



PDE5I = phosphodiesterase type 5 inhibitors.

Figure 4: Treatment algorithm of bothersome LUTS refractory to conservative/medical treatment or in cases of absolute operation indications. The flowchart is stratified by the patient's ability to have anaesthesia, cardiovascular risk, and prostate size.



(1) Current standard/first choice. The alternative treatments are presented in alphabetical order. Laser vaporisation includes GreenLight, thulium, and diode laser vaporisation. Laser enucleation includes holmium and thulium laser enucleation.
HoLEP = holmium laser enucleation; PU = prostatic urethral; TUIP = transurethral incision of the prostate; TURP = transurethral resection of the prostate.

5.5 Management of Nocturia in men with lower urinary tract symptoms

The following section reports a SR of therapy for the management of nocturia in men with LUTS. It also emphasises the need to consider the wide range of possible causes of nocturia [535].

Nocturia has been defined as the complaint of waking at night to void [5]. The ICS Standardisation Steering Committee has introduced the concept of *main sleep period*, defined as "the period from the time of falling asleep to the time of intending to rise for the next "day" [536].

Nocturia reflects the relationship between the amount of urine produced while asleep, and the ability of the bladder to store the urine received. Nocturia can occur as part of lower urinary tract dysfunction (LUTD), such as OAB and chronic pelvic pain syndrome. Nocturia can also occur in association with other forms of LUTD, such as BOO, but here it is debated whether the link is one of causation or simply the co-existence of two common conditions. Crucially, nocturia may have behavioural, sleep disturbance (primary or secondary) or systemic causes unrelated to LUTD (Table 2). Differing causes often co-exist and each has to be considered in all cases. Only where LUTD is contributory should nocturia be termed a LUTS.

Table 2: Categories of nocturia

CATEGORY	Disproportionate urine production (at all times, or during sleep)	Low volume of each void (at all times, or overnight)
Behavioural	Inappropriate fluid intake	"Bladder awareness" due to secondary sleep disturbance
Systemic	Water, salt and metabolite output	
Sleep disorder	Variable water and salt output	"Bladder awareness" due to primary sleep disturbance
LUTD		Impaired storage function and increased filling sensation

*5.5.1 **Diagnostic assessment***

Evaluation is outlined in Figure 5;

1. Evaluate for LUTD according to the relevant guidelines. The severity and bother of individual LUTS should be identified with a symptom score, supplemented by directed questioning if needed. A validated bladder diary is mandatory.
2. Review whether behavioural factors affecting fluid balance and sleep are contributing.
3. Review of medical history and medications, including directed evaluation for key conditions, such as renal failure, diabetes mellitus, cardiac failure, and obstructive sleep apnoea. If systemic factors or sleep disorders are potentially important, consider involving appropriate medical expertise (see Figure 6). This is appropriate where a known condition is sub optimally managed, or symptoms and signs suggest an undiagnosed condition.

*5.5.2 **Medical conditions and sleep disorders Shared Care Pathway***

Causative categories for nocturia comprise [537]:

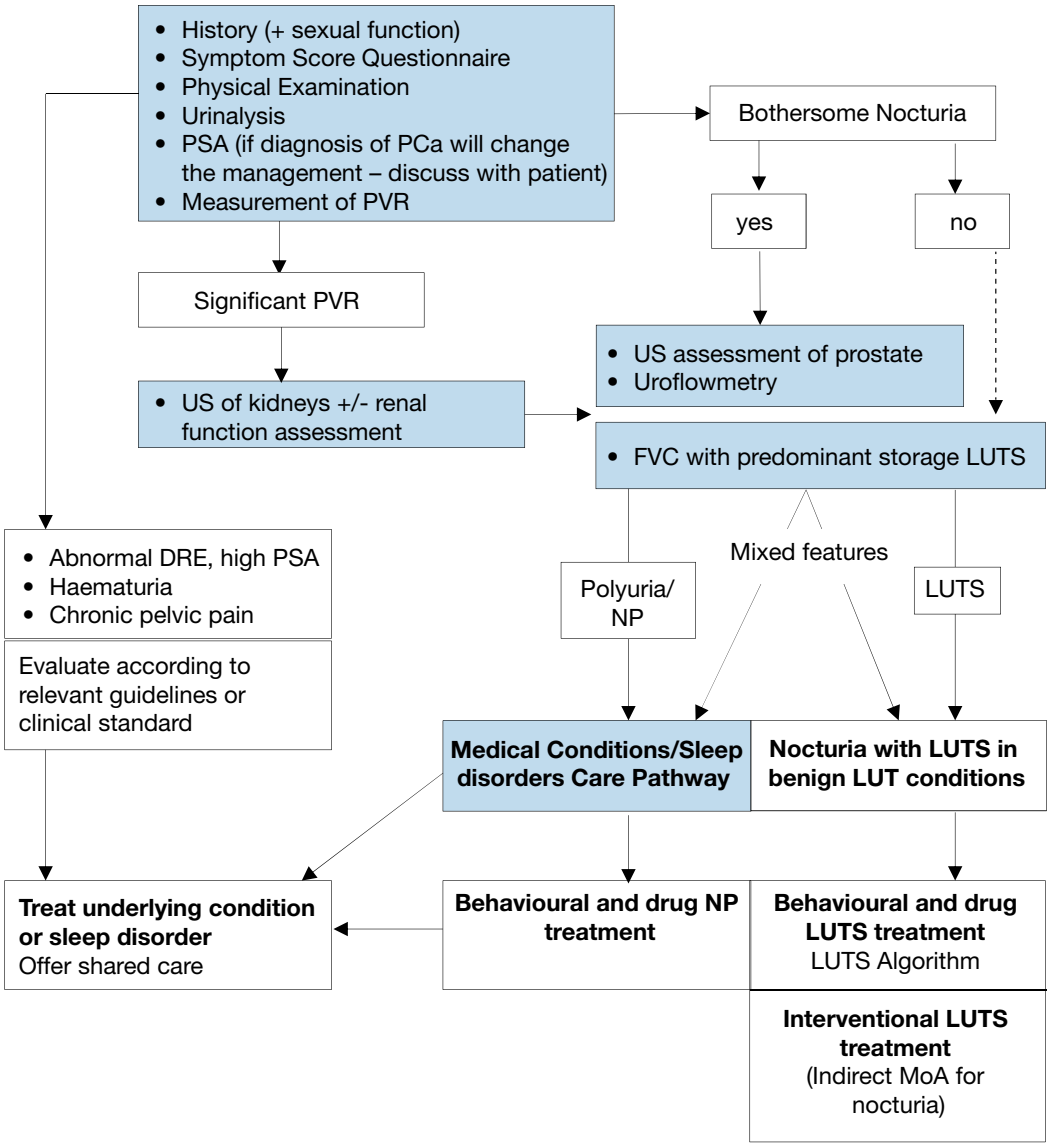
1. bladder storage problems;
2. 24-hour polyuria (> 40 mL/kg urine output over a 24-hour period);
3. nocturnal polyuria (NP; defined as excessive production of urine during the individual's main sleep period, i.e. nocturnal output exceeding 20% of 24-hour urine output in the young, or 33% of urine output in people > 65 [5]);
4. sleep disorders;
5. mixed aetiology.

Potentially relevant systemic conditions are those which impair physiological fluid balance, including influences on the levels of free water, salt, other solutes, and plasma oncotic pressure; endocrine regulation e.g., by antidiuretic hormone; natriuretic peptides; cardiovascular and autonomic control; renal function; neurological regulation, e.g., circadian regulation of the pineal gland, and renal innervation. As nocturia is commonly referred to the specialty without full insight into cause, the urologist must review the likely mechanisms underlying a presentation with nocturia and instigate review by relevant specialties accordingly. Thus, the managing urologist needs to evaluate nocturia patients in a context where additional medical expertise is available (Table 3). They should not proceed along any LUTD management pathway unless a causative link with LUTD is justifiably suspected, and systemic or sleep abnormalities have been considered.

In patients with non-bothersome nocturia, the medical evaluation (history and physical examination) should consider the possibility of early stages of systemic disease, and whether there is possibility of earlier diagnosis or therapy adjustment.

Some important potentially treatable non-urological causes of nocturia include obstructive sleep apnoea, congestive cardiac failure, poorly controlled diabetes mellitus and medications (e.g., diuretics, or lithium).

Figure 5. Evaluation of Nocturia in non-neurogenic Male LUTS.



Assessment must establish whether the patient has polyuria, LUTS, a sleep disorder or a combination. Therapy may be driven by the bother it causes, but non-bothersome nocturia may warrant assessment with a frequency volume chart (indicated by the dotted line) depending on history and clinical examination since potential presence of a serious underlying medical condition must be considered.
FVC = frequency volume chart; DRE = digital rectal examination; NP = nocturnal polyuria; MoA = mechanism of action; PVR = post-void residual; PSA = prostate-specific antigen; US = ultrasound.

Table 3: Shared care pathway for nocturia, highlighting the need to manage potentially complex patients using relevant expertise for the causative factors.

UROLOGICAL CONTRIBUTION	SHARED CARE	MEDICAL CONTRIBUTION
Diagnosis of LUTD • Urological/LUTS evaluation • Nocturia symptom scores • Bladder diary		**Diagnosis of conditions causing NP** • Evaluate patient's known conditions • Screening for sleep disorders • Screening for potential causes of polyuria*
Conservative management Behavioural therapy • Fluid/sleep habits advice • Drugs for storage LUTS • Drugs for voiding LUTS • ISC/catherisation • Increased exercise • Leg elevation • Weight loss Interventional therapy • Therapy of refractory storage LUTS • Therapy of refractory voiding LUTS	**Conservative management** • Antidiuretic • Diuretics • Drugs to aid sleep	**Management** • Initiation of therapy for new diagnosis • Optimised therapy of known conditions * Potential causes of polyuria NEPHROLOGICAL DISEASE • Tubular dysfunction • Global renal dysfunction CARDIOVASCULAR DISEASE • Cardiac disease • Vascular disease ENDOCRINE DISEASE • Diabetes insipidus/mellitus • Hormones affecting diuresis/natriuresis NEUROLOGICAL DISEASE • Pituitary and renal innervation • Autonomic dysfunction RESPIRATORY DISEASE • Obstructive sleep apnoea BIOCHEMICAL • Altered blood oncotic pressure

ISC = intermittent self catherisation

*5.5.3 **Treatment for Nocturia***

5.5.3.1 Antidiuretic therapy

The antidiuretic hormone arginine vasopressin (AVP) plays a key role in body water homeostasis and control of urine production by binding to V2 receptors in the renal collecting ducts. Arginine vasopressin increases water re-absorption and urinary osmolality, so decreasing water excretion and total urine volume. Arginine vasopressin also has V1 receptor mediated vasoconstrictive/hypertensive effects and a very short serum half-life, which makes the hormone unsuitable for treating nocturia/nocturnal polyuria.

Desmopressin is a synthetic analogue of AVP with high V2 receptor affinity and no relevant V1 receptor affinity. It has been investigated for treating nocturia [538], with specific doses, titrated dosing, differing formulations, and options for route of administration. Most studies have short follow-up. Global interpretation of existing studies is difficult due to the limitations, imprecision, heterogeneity and inconsistencies of the studies.

A SR of randomised or quasi-randomised trials in men with nocturia found that desmopressin may decrease the number of nocturnal voids by -0.46 compared to placebo over short-term follow-up (up to three months); over intermediate-term follow-up (three to twelve months) there was a change of -0.85 in nocturnal voids in a substantial number of participants without increase in major adverse events [539].

Another SR of comparative trials of men with nocturia as the primary presentation and LUTS including nocturia or nocturnal polyuria found that antidiuretic therapy using dose titration was more effective than placebo in relation to nocturnal voiding frequency and duration of undisturbed sleep [535]. Adverse events include headache, hyponatremia, insomnia, dry mouth, hypertension, abdominal pain, peripheral edema, and nausea. Three studies evaluating titrated-dose desmopressin in which men were included, reported seven serious adverse events in 530 patients (1.3%), with one death. There were seventeen cases of hyponatraemia (3.2%) and seven of hypertension (1.3%). Headache was reported in 53 (10%) and nausea in fifteen (2.8%) [535]. Hyponatremia is the most important concern, especially in patients > 65 years of age, with potential life-threatening consequences. Baseline values of sodium over 130 mmol/L have been used as inclusion criteria in some research protocols. Assessment of sodium levels must be undertaken at baseline, after initiation of treatment or dose titration and during treatment. Desmopressin is not recommended in high-risk groups [535].

Desmopressin oral disintegrating tablets (ODT) have been studied separately in the sex-specific pivotal trials CS41 and CS40 in patients with nocturia [540, 541]. Almost 87% of included patients had nocturnal polyuria and approximately 48% of the patients were > 65 years. The co-primary endpoints in both trials were change in number of nocturia episodes per night from baseline and at least a 33% decrease in the mean number of nocturnal voids from baseline during three months of treatment. The mean change in nocturia episodes from baseline was greater with desmopressin ODT compared to placebo (difference: women = -0.3 [95% CI: -0.5 to -0.1]; men = -0.4 [95% CI: -0.6 to -0.2]). The 33% responder rate was also greater with desmopressin ODT compared to placebo (women: 78% vs. 62%; men: 67% vs. 50%).

Analysis of three published placebo-controlled trials of desmopressin ODT for nocturia showed that clinically significant hyponatraemia was more frequent in patients aged ≥ 65 years than in those aged < 65 years in all dosage groups, including those receiving the minimum effective dose for desmopressin (11% of men aged ≥ 65 years vs. 0% of men aged < 65 years receiving 50 mcg; 4% of women ≥ 65 aged years vs. 2% of women aged < 65 years receiving 25 mcg). Severe hyponatraemia, defined as ≤ 125 mmol/L serum sodium, was rare, affecting 22 of 1,431 (2%) patients overall [542].

Low-dose desmopressin ODT has been approved in Europe, Canada and Australia for the treatment of nocturia with ≥ 2 episodes in gender-specific low doses 50 mcg for men and 25 mcg for women; however, it initially failed to receive FDA approval, with the FDA citing uncertain benefit relative to risks as the reason. Following resubmission to the FDA in June 2018 desmopressin acetate sublingual tablet, 50 mcg for men and 25 mcg for women, was approved for the treatment of nocturia due to nocturnal polyuria in adults who awaken at least two times per night to void with a boxed warning for hyponatremia.

Desmopressin acetate nasal spray is a new low-dose formulation of desmopressin and differs from other types of desmopressin formulation due to its bioavailability and route of administration. Desmopressin acetate nasal spray has been investigated in two RCTs including men and women with nocturia (over two episodes per night) and a mean age of 66 years. The average benefit of treatment relative to placebo was statistically significant but low, -0.3 and -0.2 for the 1.5 mcg and 0.75 mcg doses of desmopressin acetate, respectively. The number of patients with a reduction of more than 50% of nocturia episodes was 48.5% and 37.9%, respectively compared with 30% in the placebo group [543]. The reported adverse event rate of the studies was rather low, and the risk of hyponatremia was 1.2% and 0.9% for desmopressin acetate 1.5 mcg and 0.75 mcg, respectively. Desmopressin acetate nasal spray was approved by the FDA in 2017 for the treatment of nocturia due to nocturnal polyuria, but it is not available in Europe.

Practical considerations: A complete medical assessment should be made, to exclude potentially non-urological underlying causes, e.g., sleep apnoea, before prescribing desmopressin in men with nocturia due to nocturnal polyuria. The optimal dose differs between patients, in men < 65 years desmopressin treatment should be initiated at a low dose (0.1 mg/day) and may be gradually increased up to a dosage of 0.4 mg/day every week until maximum efficacy is reached. Desmopressin is taken once daily before sleeping. Patients should avoid drinking fluids at least one hour before and for eight hours after dosing. Low dose desmopressin may be prescribed in patients > 65 years. In men ≥ 65 years or older, low dose desmopressin should not be used if the serum sodium concentration is below normal: all patients should be monitored for hyponatremia. Urologists should be cautious when prescribing low-dose desmopressin in patients under-represented in trials (e.g., patients > 75 years) who may have an increased risk of hyponatremia.

5.5.3.2 Medications to treat LUTD

Where LUTD is diagnosed and considered causative of nocturia, relevant medications for storage (and voiding) LUTS may be considered. Applicable medications include; selective α1-adrenergic antagonists [544], antimuscarinics [545-547], 5-ARIs [548] and PDE5Is [549]. However, effect size of these medications is generally small, or not significantly different from placebo when used to treat nocturia [535]. Data on OAB medications (antimuscarinics, beta-3 agonist) generally had a female-predominant population. No studies specifically addressing the impact of OAB medications on nocturia in men were identified [535]. Benefits with combination therapies were not consistently observed.

5.5.3.3 Other medications

Agents to promote sleep [550], diuretics [551], non-steroidal anti-inflammatory agents (NSAIDs) [552] and phytotherapy [553] were reported as being associated with response or QoL improvement [535]. Effect size of these medications in nocturia is generally small, or not significantly different from placebo. Larger responses have been reported for some medications, but larger scale confirmatory RCTs are lacking. Agents to promote sleep do not appear to reduce nocturnal voiding frequency but may help patients return to sleep.

Summary of evidence	LE
No clinical trial of pathophysiology-directed primary therapy has been undertaken.	4
No robust clinical trial of behavioural therapy as primary intervention has been undertaken.	4
Antidiuretic therapy reduces nocturnal voiding frequency in men with baseline severity of two or more voids per night.	1b
There is an increased risk of hyponatremia in patients 65 years of age or older under antidiuretic therapy.	1b
Antidiuretic therapy increases duration of undisturbed sleep.	1b
Alpha 1-blocker use is associated with improvements in undisturbed sleep duration and nocturnal voiding frequency, which are generally of only marginal clinical significance.	2
Antimuscarinic medications can reduce night-time urinary urgency severity, but the reduction in overall nocturia frequency is small or non-significant.	2
Antimuscarinic medications are associated with higher incidence of dry mouth compared with placebo.	2
5α-reductase inhibitors reduce nocturia severity in men with baseline nocturia severity of two or more voids per night.	2
A trial of timed diuretic therapy may be offered to men with nocturia due to nocturnal polyuria. Screening for hyponatremia should be undertaken at baseline and during treatment.	1b

Recommendations	Strength rating
Treat underlying causes of nocturia, including behavioural, systemic condition(s), sleep disorders, lower urinary tract dysfunction, or a combination of factors.	Weak
Discuss behavioural changes with the patient to reduce nocturnal urine volume and episodes of nocturia and improve sleep quality.	Weak
Offer desmopressin to decrease nocturia due to nocturnal polyuria in men < 65 years of age.	Weak
Offer low dose desmopressin for men > 65 years of age with nocturia at least twice per night due to nocturnal polyuria.	Weak
Screen for hyponatremia at baseline, day three and day seven, one month after initiating therapy and periodically during treatment. Measure serum sodium more frequently in patients > 65 years of age and in patients at increased risk of hyponatremia.	Strong
Discuss with the patient the potential clinical benefit relative to the associated risks from the use of desmopressin, especially in men > 65 years of age.	Strong
Offer α1-adrenergic antagonists for treating nocturia in men who have nocturia associated with LUTS.	Weak
Offer antimuscarinic drugs for treating nocturia in men who have nocturia associated with overactive bladder.	Weak
Offer 5α-reductase inhibitors for treating nocturia in men who have nocturia associated with LUTS and an enlarged prostate (> 40 mL).	Weak
Do not offer phosphodiesterase type 5 inhibitors for the treatment of nocturia.	Weak

5.6 Management of male urinary incontinence

The aim of the following section is to provide evidence-based recommendations for the management of male UI.

5.6.1 Epidemiology and Pathophysiology

Urinary incontinence is defined as an unintentional loss of urine and is reported to have a prevalence of 11% in men aged 60 to 64 years old to 31% in men ≥ 85 years and to affect up to 32% of men with LUTS [554-556]. Urinary incontinence can be further classified into three types: SUI, UUI and mixed urinary incontinence (MUI). Overflow urinary incontinence, post-micturition dribble, nocturnal enuresis, and total incontinence are specific forms of UI that are outside the current scope of this guideline. An overview of the epidemiology and pathophysiology of male UI is given in table 4.

Table 4: Epidemiology and pathophysiology overview of male UI [556-560].

Type	Definition	Causes and associated factors	Pathophysiology	Clinical presentation
Stress UI: prevalence < 10%	Urine loss during movement or efforts or in general during increased abdominal pressure.	• Benign Prostatic Obstruction surgery • Neurogenic condition • Pelvic surgery • Radical prostatectomy • Urethral surgery	Sphincter deficiency	**Symptoms:** UI during physical activity, exercises, e.g. during coughing, sneezing, no leakage during sleep, no nocturnal enuresis **Voiding diary/Pad test:** with activity **Cough stress test:** leakage can coincide with coughing
Urgency UI: prevalence 40-80%	Urine loss concomitant or immediately following an urgency episode.	• Ageing process • Anorectal dysfunction/GI disorders • Behavioural factors (fluid intake and caffeine consumption) • Chronic BPO • Idiopathic • Intrinsic bladder diseases (cystitis, fibrosis, interstitial cystitis) • Metabolic syndrome • Neurogenic conditions • UTIs	• Detrusor overactivity (neurogenic or not) • Urothelial stimulation • Increased afferent signalling • Others (pelvic organ cross talk, bladder wall ischemia etc.)	**Symptoms:** urgency, usually associated with, increased frequency and nocturia **Voiding diary:** urgency, frequency and nocturia
Mixed UI: prevalence 10-30%	Any combination of SUI and UUI.	Causes of both SIU and UUI	Combination of SUI and UUI	**Symptoms:** UI equally as often with physical activity as with a sense of urgency **Voiding diary:** varies **Cough stress test:** may show leakage with coughing

BPO = benign prostatic obstruction; GI = gastrointestinal; SUI = stress urinary incontinence; UI = urinary incontinence; UTI = urinary tract infection; UUI = urgency urinary incontinence

*5.6.2 **Diagnostic Evaluation***

Medical history and physical examination of males with UI is the same as for male LUTS and should allow UI to be categorised into SUI, UUI or MUI and to identify other types of UI (overflow UI, nocturnal enuresis), or those who need rapid referral to an appropriate specialist (e.g., pelvic diseases, neurological conditions).

Specific validated questionnaires can help to quantify UI severity; however, a detailed description of the different urinary symptoms questionnaires and PROMs is beyond the scope of this guideline. For more information on available questionnaires see the 6th ICI review on patient reported outcomes assessment [561].

Voiding diaries are a standardised method of measuring symptom severity, including frequency and extent of UI episodes, voided volume and 24-hour or nocturnal total urine volume [43].

Pad tests can be used to quantify severity of UI and to monitor patient's response to treatment although the usefulness of these tests in predicting outcome of treatment is uncertain. Despite this, early post-operative testing with pad tests may predict future continence in men after prostatectomy [562, 563].

Urodynamic testing (multichannel cystometry, video-urodynamics) and specific tests of urethral function (urethral pressure profilometry, Valsalva leak point pressure, retrograde urethral resistance) should be considered on an individual basis, such as in cases when invasive treatment is considered. A Cochrane review showed that use of urodynamic tests increased the likelihood of prescribing drugs or avoiding surgery, while there is limited evidence that it should be used for the assessment of post prostatectomy UI [561].

Post-void residual volume measurement can be applied with caution to men with non-neurogenic UI, as the prevalence, severity, and clinical application of PVR in men with UI is uncertain.

Imaging (US, MRI, CT scan) can improve the understanding of the anatomical and functional abnormalities that may cause UI and thus help its management [564].

Urinalysis: Reagent strip ('dipstick') urinalysis may indicate UTI, proteinuria, haematuria, or glycosuria, requiring further tests as recommended according to other EAU Guidelines, e.g., Guidelines on urinary tract cancers and urological infections [48-51].

Summary of evidence	LE
Validated specific symptom score questionnaires and voiding diaries assist in the screening for and categorisation of UI.	3
Pad test can be used to quantify the presence and severity of UI, as well as a patient's response to treatment.	3
There is limited evidence that urodynamics and PVR affect treatment choice in men with uncomplicated UI.	3

Recommendation	Strength rating
Take a complete medical history including symptoms and co-morbidities, medications, and a focused physical examination in the evaluation of men with urinary incontinence (UI).	Strong
Use a validated symptom score questionnaire, bladder diary and pad-test to assess UI.	Strong
Measure post-void residual in the assessment of UI.	Strong
Perform urodynamics for UI when considering invasive treatment.	Weak

*5.6.3 **Conservative treatment***

5.6.3.1 Simple clinical interventions

5.6.3.1.1 Lifestyle interventions

Examples of lifestyle factors that may be associated with UI include obesity, smoking, level of physical activity and diet. Modification of these factors may improve UI, but most of the evidence for these interventions come from studies with predominately female study populations. However, as many of these interventions are now generalised public health measures their recommendation is in line with general medical practice [565-567].

Modification of fluid intake, particularly restriction, is a strategy commonly used by people with UI to relieve symptoms. Advice on fluid intake given by healthcare professionals should be based on 24-hour fluid intake and urine output measurements. From a general health point of view, it should be advised that fluid intake should be sufficient to avoid thirst and that low or high 24-hour urine output should be investigated [565, 568]. A cross-sectional population survey found no statistical association between caffeine intake and UI [569]. Conversely, an RCT showed that reduction of caffeine intake, associated with behavioural therapy, resulted in reduced urgency but not UI compared to behavioural therapy alone [570].

5.6.3.1.2 Treatment of co-morbidities

Urinary incontinence, especially in the elderly, has been associated with multiple co-morbid conditions [571]. It is possible that improvement of associated disease may reduce the severity of urinary symptoms. However, this is often difficult to assess as patients frequently suffer from more than one condition. Interventions may be combined and individualised, making it impossible to decide which alteration in an underlying disease has affected a patient's UI.

In patients with existing UI, particularly the elderly, it may be difficult or impossible to distinguish between the effects of medication, co-morbidities or ageing on UI. Although changing drug regimens for underlying diseases may be considered as a possible early intervention, there is limited evidence of benefit [572]. There is also a risk that stopping or altering medication may result in greater harm than benefit.

5.6.3.1.3 Constipation

One RCT, with a majority female population, found that a multimodal intervention in elderly patients, involving assisted toileting, fluid intake, etc., reduced the occurrence of UI and constipation, while behavioural therapy appeared to improve both [573]. However, there is no evidence to show whether treating constipation improves UI, although both constipation and UI appear to be improved by certain behavioural interventions.

5.6.3.1.4 Containment

Containment includes the use of absorbent pads, urinary catheters, external collection devices and penile clamps. A SR of six RCTs comparing different types of pads found that pads filled with super absorbent material were better than standard pads [574]. For men with light UI, a randomised crossover trial found that a leaf-shaped type of pad was preferred to rectangular pads [575].

A Cochrane review compared different types of long-term indwelling catheters and found no evidence that one catheter material or type of catheter was superior to another [576]. A SR of non-randomised studies found no differences in UTI outcome or Upper Urinary Tract (UUT) changes between use of suprapubic or urethral catheter drainage; however, patients with suprapubic catheters were less likely to have urethral complications [577]. For people using intermittent catheterisation, a Cochrane review found no evidence that one type of catheter or regimen of catheterisation was better than another [578].

An RCT in 56 men with post-prostatectomy incontinence (PPI) compared sheath drainage system, body-worn urinal, penile clamp, and absorbent pads. It was found that the three devices and absorbent pads have different strengths and limitations that make them more (or less) suitable for particular activities. Most men prefer to use a combination of devices and pads to meet their lifestyle needs. Hinge-type penile clamp was good for short vigorous activities as it was the most secure, least likely to leak and most discreet, although almost all men described it as uncomfortable or painful [579].

Summary of evidence	**LE**
There is limited evidence that lifestyle interventions e.g., weight reduction, smoking cessation or diet modification improves UI in males.	3
There is limited evidence that improving co-morbidities or changing drug regimens for underlying disease improves UI in males.	3
Pads and/or penile sheaths are palliative options for management of UI.	1b

Recommendation	**Strength rating**
Offer lifestyle advice that may improve urinary incontinence (UI) to patients; however, patients should be informed that the evidence for these interventions is lacking.	Weak
Review any medication associated with the development or worsening of UI.	Weak
Use pads and/or penile sheaths as a palliative option for the management of UI.	Weak

5.6.3.2 Behavioural and Physical therapies

Behavioural and physical therapies encompass all treatments which require a form of self-motivated personal retraining by the patient and include techniques that are used to augment this effect. Usually in clinical practice, these will be introduced as part of a package of care including lifestyle changes, patient education, and possibly cognitive therapy as well. Further details for behavioural treatments are outlined in section 5.1.2 of these guidelines.

5.6.3.2.1 Prompted or timed voiding

With prompted voiding, carers rather than the patient, initiate the decision to void. Two SRs confirmed a positive effect on continence outcomes for prompted voiding in comparison to standard care [580, 581]. Timed voiding is defined as fixed, pre-determined, time intervals between toileting, applicable for those with or without cognitive impairment. A Cochrane review of timed voiding, included two RCTs, found inconsistent improvement in continence compared with standard care in cognitively impaired adults [582].

5.6.3.2.2 Bladder training

Bladder training goals are to correct faulty habit patterns of frequent urination, improve control over bladder urgency, prolong voiding intervals, increase bladder capacity, reduce incontinent episodes, and restore patient

confidence in controlling bladder function. The ideal form or intensity of a BT program for UI is unclear. It is also unclear whether BT can prevent the development of UI. The addition of BT to anticholinergic therapy did not improve UI compared to antimuscarinics alone but it did improve frequency and nocturia [583]. In seven RCTs, BT was compared to drug therapy alone, and showed only a benefit for oxybutynin in cure and improvement of UI [583].

5.6.3.2.3 Pelvic floor muscle training

A 2015 Cochrane review concluded that there was no overall benefit at twelve months post-surgery for men who received post-operative pelvic floor muscle training (PFMT) for the treatment of PPI and that the benefits of conservative treatment of PPI remain uncertain [584]. However, a subsequent SR and meta-analysis showed that PFMT either alone or in combination with biofeedback and/or electrical stimulation was effective for treating PPI, significantly reducing the time to continence recovery [585]. A further meta-analysis demonstrated that the addition of guided programs using biofeedback and/or pelvic floor muscle electric stimulation (PFES) significantly improved continence recovery rates at one- and three-month intervals post-surgery compared to PFMT alone [586].

Two subsequent SRs in patients who underwent robotic-assisted radical prostatectomy demonstrated that the addition of PFMT to the post-operative management plan shorten the time to continence recovery [587, 588].

Two RCTs have shown that written instructions alone offer similar levels of improvement to supervised PFMT [589, 590]. One RCT found that PFMT was helpful in men who had been incontinent for at least one year after prostatectomy, and who had had no previous therapy [591].

One RCT compared PFMT to no treatment in men undergoing TURP. There was no demonstrable difference in the incidence of post-operative incontinence up to twelve months [592]. On the other hand, an RCT in men who underwent HoLEP, demonstrated that PFMT when started pre-operatively promoted early recovery of continence [593].

Other RCTs demonstrated that like PFMT, increased pelvic floor muscle strength and quicker return to continence may be achieved with the Pilates method [594], the oscillating rod [595], a combination of biofeedback with electrostimulation [596] and whole body vibration training [597]. Furthermore, quicker return to continence and improved QoL may be achieved, even with extended and continuing nursing care [598].

5.6.3.2.4 Electrical stimulation

The majority of evidence on electrical stimulation refers to women with SUI and many are generally low quality, with a variety of stimulation parameters, treatment regimens and outcome parameters [592].

An RCT of 70 PPI men receiving surface or intra-anal electrostimulation reported a significant reduction in UI in terms of grams of urine loss and a significant improvement in QoL from baseline, but no statistically significant difference between treatment arms [599].

A Cochrane review of six RCTs on electrical stimulation in men with UI concluded that there was some evidence that electrical stimulation enhanced the effect of PFMT in the short-term but not after six months. Electrical stimulation was also more effective than sham stimulation at six, but not twelve months; however, there were more adverse effects including pain and discomfort with electrical stimulation [600].

Electromagnetic stimulation has been promoted as a treatment for UI, but only weak evidence of the short- and long-term effects has been reported in SRs [601, 602].

5.6.3.2.5 Posterior tibial nerve stimulation

Posterior tibial nerve stimulation (PTNS) has been studied as a treatment of UI, especially UUI. Electrical stimulation of the posterior tibial nerve delivers electrical stimuli to the sacral micturition centre via the S2-S4 sacral nerve plexus. Stimulation is done either percutaneously using a fine, 34-G, needle, inserted just above the medial aspect of the ankle (P-PTNS) or transcutaneously using surface electrodes (T-PTNS). Percutaneous-PTNS treatment cycles typically consist of twelve weekly treatments of 30 minutes and T-PTNS treatment cycles typically consists of self-administered, twenty-minute daily sessions, after adequate education.

A female-predominant sham controlled RCT, assessed the effectiveness of PTNS in OAB population. There were 22.8% and 20% males in the treatment and sham arms, respectively [603]. Overactive bladder symptoms improved significantly in 54.5% of patients in the PTNS arm compared to 20.9% in the sham arm. A non-inferiority RCT comparing T-PTNS compared to P-PTNS, reported significant improvements in daytime frequency, urgency and UUI episodes without significant difference between treatment arms after twelve weeks of therapy [604]. A SR on T-PTNS in idiopathic and neurogenic female-predominant (males < 10%) population, reported significant improvement in OAB symptoms in 48-93% of patients and cure of UUI episodes in 25-45% [605].

For PTNS, mild pain and discomfort at the puncture site is the most common adverse event [606]. Small hematomas, swelling, leg tingling and vasovagal reaction to needle placement have also been reported [603]. Treatment adherence is generally high at 89.7% [604]. Contra-indications include a cardiac pacemaker and skin disease at the site of stimulation.

There is some evidence that PTNS may benefit male patients with OAB, but due to too insufficient data, no recommendation on PTNS in males can be made at this time. However, considering the safety of this therapy, it can be offered to male patients as an alternative option prior to more invasive treatments.

Summary of evidence	LE
Prompted voiding, either alone or as part of a behavioural modification programme, improves continence in elderly, care-dependent people.	1b
The combination of bladder training (BT) with antimuscarinic drugs does not result in greater improvement of UI but may improve frequency and nocturia.	1b
There is conflicting evidence on whether the addition of BT, electrostimulation or biofeedback increases the effectiveness of PFMT alone.	1b
Pre-operative PFMT does not confer additional benefit to men undergoing radical prostatectomy.	1b
Electrical stimulation may add benefit to PFMT up to six months.	2
Electrical stimulation may improve UI compared to sham up to six months.	2
There is limited evidence for the effectiveness of PTNS in male population.	2
There is no evidence that PTNS cures UUI in male population.	2

Recommendations	Strength rating
Implement prompted voiding for patients with urinary incontinence (UI) where appropriate.	Strong
Offer bladder training as a complementary treatment for UI.	Weak
Offer pelvic floor muscle training alone or in combination with biofeedback and/or electrostimulation to men undergoing radical prostatectomy to speed recovery from UI.	Weak

*5.6.4 **Pharmacological management***

5.6.4.1 Drugs for urgency urinary incontinence

Muscarinic receptor antagonists [607-610] and beta-3 agonist [297-299, 611-614] are currently the first-line pharmacological treatments for UUI. The mechanism of action, efficacy, and safety and tolerability profiles of both classes of drugs are discussed in detail in sections 5.2.3 and 5.2.4, respectively.

5.6.4.2 Drugs for stress urinary incontinence

A SR of eight studies evaluating the efficacy of duloxetine in postprostatectomy SUI reported that duloxetine resulted in a mean dry rate of 58% (25–89%), mean improvement in pad number of 61% (12–100%), and mean improvement in one-hour pad weight of 68% (53–90%), at short-term follow-up (mean one to nine months) [615]. However, mean adverse event rates were high, and treatment was discontinued in 38% of cases. The overall certainty of the evidence was low due to study heterogeneity and methodological limitations. Further RCTs with long-term follow-up are required.

Summary of evidence	LE
Antimuscarinic monotherapy can significantly improve urgency, UUI, and increased daytime frequency.	1b
Mirabegron is superior to placebo and as efficacious as antimuscarinics for improvement of UUI.	1b
Duloxetine led to a short-term improvement in postprostatectomy SUI symptoms and QoL improvement; however, a significant proportion of men discontinued treatment.	1b

Recommendations	Strength rating
Offer antimuscarinic drugs or mirabegron to adults with urge urinary incontinence who failed conservative treatment.	Strong
Offer duloxetine to men with stress urinary incontinence.	Weak
Inform patients about the possible adverse events of duloxetine and that its use is off label for this indication in Europe.	Strong

5.6.5 *Surgical treatment for stress urinary incontinence*

5.6.5.1 *Bulking agents in men*

Mechanism of Action: Urethral bulking agents work by adding bulk and improving the coaptation of a damaged sphincter zone. They represent a treatment option for men with either small volume leak or for those unfit for more invasive treatment options [616].

Efficacy: A Cochrane review on surgical treatment of PPI identified only one RCT that fulfilled the inclusion criteria. This trial randomised 45 men to Macroplastique injection or artificial urinary sphincter (AUS) implantation and compared their outcomes at 48 months [616]. Significant improvement was reported in both groups for men with minimal incontinence, but in men with total incontinence there was a significant difference in continence rates favouring AUS implantation (72% vs. 23%) [617]. A SR of eight studies (n=142) in men using Macroplastique, Opsys, Durasphere and Urolastic, showed short-term improvement, and reported dry rates between 0-83% [616]. A propensity score-matched analysis of 104 men with PPI, compared submucosal injection of Macroplastique to transobturator male sling (TiLOOP male) [618]. At twelve months follow-up, the reported failure free rates were 15.4% and 76.9%, the daily use of 0-1 pads was 21.2% and 67.3% and the satisfaction rate was 3.8% and 71.2%, respectively. Several small cohort studies of several different bulking agents have not shown any benefit.

A narrative review including data from 25 articles, reports a success rate with all bulking procedures of 54.3%, with 37.5% of symptoms improvement and almost 30% of dryness [619].

In a SR and meta-analysis, three studies addressed bulking agents. Two of them, involving a total of 384 participants, showed a pooled short-term cure rate of 26.1% and a single study on 68 subjects reported a 10.3% long term cure rate. Short- and long-term reoperation rates were not described [620].

Tolerability and safety: Bulking agent associated dysuria and haematuria are frequently reported to be transient and self-resolving [616]. The risk of urinary retention requiring clean intermittent self-catheterisation (CISC), or long-term catheter use is minimal [621]. However, they may provoke allergic reactions [622] and carry a potential risk for migration [623] to proximal and distal lymph nodes [624]. Overall, post procedural urinary retention rates range between 3-17%, with rare need for temporary catheterisation, while post-operatory urinary tract infections ranged from 6-7% [619].

Practical considerations: Bulking agents have shown low cure rates but remain an option for men unfit for more invasive treatment options.

Summary of evidence	**LE**
There is very limited evidence that bulking agents are effective for the treatment of PPI.	2

Recommendation	**Strength rating**
Do not offer bulking agents to men with post-prostatectomy incontinence.	Weak

5.6.5.2 *Male Slings*

Male slings have been introduced to treat mild-to-moderate PPI. However, the definitions of mild and moderate UI are unclear. The majority of studies define cure as ‘no pad use’ or ‘one security pad per 24-hours’. Some authors used more strict criteria such as ‘urine loss of less than 2 g per 24-hour pad test’ [625].

5.6.5.2.1 Non-adjustable slings

Mechanism of Action: Non-adjustable male slings are positioned under the urethra and fixed by a retropubic or transobturator approach. The tension is adjusted during the surgery, and it cannot be re-adjusted post-operatively. Synthetic slings restore continence in males either by urethral compression and/or by repositioning the bulb of urethra [626, 627].

Efficacy: A SR and meta-analysis involving 33 prospective cohorts and one RCT comparing sling to AUS, reported that both options are effective in improving UI and QoL [628]. Following sling insertion, the overall cure rate was 60% (95% CI: 0.51-0.67) and 56% (95% CI: 0.44-0.68) for sling and AUS respectively. The 24-hour pad use was -3.33 (95% CI: -4.33 to -2.34) and -3.75 (95% CI: -4.56 to -2.93) for slings and AUS, respectively. Similar findings were reported by a network meta-analysis that showed comparable efficacy between slings and AUS [629].

The MASTER Trial, a non-inferiority RCT comparing the outcomes of continence surgery in men with bothersome urodynamic SUI, using a very strict definition of UI after prostate surgery, reported that at twelve-

months incontinence rates were 87% for male sling vs. 84.2% for AUS (95% CI: -11.6-4.6, P_{NI}=0.003), confirming non-inferiority [630]. The subgroup analysis suggested that male sling is inferior to AUS for men with greater incontinence at baseline (pad weight > 250g); however, the difference did not reach statistical significance.

For the re-positioning slings (AdVance™ and AdVanceXP©), a mean subjective cure rate of 49% (8.6-73.7%) after mean follow-up of three years has been reported for 136 patients [631]. A prospective multicentre cohort study, with 60-month follow-up, in men with AdVanceXP demonstrated a constant continence outcome over time with a 57.6% cure rate, 25.4% improvement rate and 16.9% failure rate. These findings were verified in an additional study which reported cure rates of 66.7% and 71.7%, improvement rates of 26.5% and 24.4% and failures rates of 6.9% and 13.3% at 24- and 48-months, respectively [632]. A retrospective comparative study showed that both options are safe and effective in the treatment of male SUI [633].

With the transobturator compressive I-Stop TOMS male sling, 38% of men were dry at twelve months, but this reduced to 23% and 15% after four and five years, respectively [634].

Tolerability and safety: A SR and meta-analysis of 1,170 men with SUI and male sling, demonstrated that the predictors of failure are prior radiation, severity of incontinence and previous surgeries [635]. Pelvic radiotherapy has also been reported in other studies as a negative prognostic factor [636]. A comparison among radiated vs. non-radiated men who had AdVanceXP reported a greater degree of post-operative improvement in the non-radiated group (49.6% vs. 22.2%) as well as greater satisfaction rates (95% vs. 64%) [637]. The most common complication with male slings is pain and local superficial wound infection [638]. Chronic pain has been observed in 1.3% of men who had non-adjustable slings [638]. Post-operative transient voiding dysfunction occurred in 4.3-10.3%, mostly as *de novo* urgency or urinary retention, while erosions and chronic pain were uncommon (0-0.4%), as was explantation [631, 632, 639-641].

Practical considerations: Fixed male slings are considered safe and improve continence, but their efficacy is limited in men with severe incontinence or previous radiotherapy.

5.6.5.2.2 Adjustable slings in males

Mechanism of Action: Adjustable slings in males are those for which the tension of the sling can be adjusted post-operatively. Three main systems have been used in men: the Remeex® system [642], the Argus® system [643] and the ATOMS® system [644].

Efficacy: There is one small RCT for adjustable slings in males [645]. Most studies consist of prospective or retrospective case series, with variable follow-up and different definitions of success [642, 644-648]. A SR reported objective cure rates varying between 17-92% after adjustable sling implantation [638].

For the Remeex® system, only two studies, with conflicting findings, have been published. One study followed nineteen patients for nearly seven years and reported 70% success, with no explants, infections, or erosions [642]. The second study followed fourteen patients for 25 months. Only 36% of patients were satisfied and multiple re-adjustments were needed. Mechanical failure was reported in 21% [646].

Data on the Argus® system has been reported for 404 men, but only few series have reported on more than 40 patients, with the longest follow-up being 35-months. Success rates varied between 17-93%, with a mean of 73.0% reporting subjective cure [647, 648]. A head-to-head comparison between the two Argus systems reported similar efficacy outcomes at 44 months, but Argus T was associated with a higher inguinal pain and explantation rate [649]. A small study of 22 men with PPI randomised to AdVance or Argus T reported superior 24-hour pad test results and of patient satisfaction levels for Argus T at eighteen-months follow-up [645].

A SR of the ATOMS® system reported the pooled evidence from 1,393 patients with a 67% dryness, 90% improvement after adjustment and 16.4% complication rate [644]. The expulsion rate was 5.75%. Another SR and meta-analysis with 3,059 patients reported that ATOMS® was superior to ProACT in mean dryness rate (68% vs. 55%), overall improvement (91% vs. 80%), satisfaction rate (87% vs. 56%), mean number of filing adjustments (2.4 vs. 3.5) and post-operative pad use per day (1.1 vs. 2.1) [650].

Tolerability and Safety: The most frequent complications in adjustable male slings are pain, erosions, and infections [638]. Pain at the implant site was usually only temporary, but chronic pain has been reported in 1.5% of men [647, 648]. The number of implants requiring re-adjustment is reported between 8-38.6% [648, 651, 652]. Explantation rates range from 10-15.8% and erosion rate is estimated around 10% [635]. The most common

reasons for explantation are device infection (4.1-8%), erosions (4-12%), and urethral perforations (2.7-16%). A SR reported a device explantation rate of 5% vs. 25% and a major complication rate of 4.2% vs. 10.4% for ATOMS® and ProACT, respectively [650].

Practical considerations: There is no evidence that adjustability offers additional benefit as RCTs are lacking; therefore, no recommendation can be made at this time. Explantation rate seems superior to fixed male sling based on external comparisons.

5.6.5.2.3 Autologous slings

The strategy of intra-operative placement of an autologous vas deferens sling below the vesico-urethral anastomosis during robotic-assisted radical prostatectomy (RARP) has been explored with the intention to improve early return of continence. Two RCTs [653, 654] showed an advantage of sling vs. no sling at one-month follow-up, and another study [655] showed an advantage of a 6-branch vs. a 2-branch sling at one month follow-up. However, a larger RCT (n=195), showed that continence rate and near-continence rate were similar between groups at six months with 66% vs. 65% and 86% vs. 88%, respectively [656].

Summary of evidence	**LE**
There is limited short-, medium- and long-term evidence that fixed transobturator male slings cure or improve PPI in patients with mild-to-moderate incontinence.	1b
Men with severe incontinence, previous radiotherapy or transurethral surgery may have less benefit from fixed transobturator male slings.	2
There is limited evidence that adjustable male slings can cure or improve SUI in men.	3
There is no evidence that adjustability offers additional benefit over other types of slings.	3
There is no evidence that intra-operative placement of an autologous sling during RARP improves return of continence at six months.	1b

Recommendations	**Strength rating**
Offer non-adjustable transobturator slings to men with mild-to-moderate* post-prostatectomy incontinence.	Weak
Inform men that severe incontinence, prior pelvic radiotherapy or transurethral surgery may worsen the outcome of non-adjustable male sling surgery.	Weak

** The terms "mild" and "moderate" PPI remain undefined.*

5.6.5.3 Compression devices in males

5.6.5.3.1 Artificial urinary sphincter

Mechanism of action: The AUS is the standard treatment for moderate-to-severe male SUI. The AMS 800 three component system with inflatable cuff, control pump and pressure regulating balloon is the device with the longest follow-up and the greatest level of evidence [657]. The ZSI 375 is a two-component device, inflatable cuff, and control pump, allowing an easier implantation process [658]. Other AUS devices have been launched e.g., the Victo and Br-SL-AS 904 systems but robust evidence regarding their efficacy and safety is pending [659].

Efficacy: A meta-analysis of 33 cohort studies and one RCT, reported significant improvement after AUS implantation in overall cure rates (56%) and reductions in pad used per 24-hours (-3.75) [628]. Several observational studies reported on functional outcomes after AMS 800. Social continence rates (0-1 pads used daily) ranged from 55-76.8% [660-662]. A 77.2% continence rate and 89.5% subjective satisfaction rate have been reported after a median follow-up of > 15 years in 57 men who had undergone AUS placement [663]. A prospective cohort study of 40 patients with a mean follow-up of 53 months, showed that from all urodynamic parameters only low bladder compliance had a negative impact on outcome [664]. However, another retrospective study showed that no urodynamic factors adversely altered the outcome of AUS implantation [665]. Some recent multicenter studies have confirmed older statements that surgeon's experience and higher surgical volume is associated with better outcomes and a lower revision rate after AUS implantation [666, 667].

The data regarding ZSI 375 is limited. A retrospective, non-randomised trial across several centres in Europe, reported an 84.4% success rate (19.3% dry rate and 65.1% improved 0-1 pads per day) after 43 months [658]. A 72% success rate was reported at seven years follow-up for 45 patients who underwent placement of the ZSI 375 device in France [668].

Tolerability and safety: Artificial urinary sphincter complications include device infection/erosion (8.5%), mechanical failure (6.2%) and urethral atrophy (7.9%) [669]. In multivariate analysis, radiation therapy was

independently associated with risk of urethral atrophy, as were older age and a longer time interval between prostate cancer treatment and AUS surgery [662]. Urethral erosion is associated with previous irradiation and penoscrotal approach [670]. The reported revision rates at three years for any reason were 10-29.1% [660, 670-672]. The risk of urethral erosion after ZSI 375 AUS is 8.2-13.3% and risk of mechanical failure is 2.2-2.5% [658].

Practical Considerations: Artificial urinary sphincter is efficacious and improves the QoL of men with PPI. To minimise complications, it is advised to refer patients to specialised centres experienced in AUS implementation. Men considering insertion of an AUS should be fully informed that the success of the intervention relies on their ability to operate the pump. Treating physicians should keep in mind that operating the AUS may become difficult in men who develop cognitive impairment or lose manual dexterity. Artificial urinary sphincter has a limited lifespan and 'maintenance' re-operations are common in the long-term. These re-interventions should not be classified as complications [657].

5.6.5.3.2 Non-circumferential compression device (ProACT®)

Mechanism of action: The ProACT® system consists of two devices. Each device includes the balloon, the bi-lumen tubing, and the volume-adjustment port. The devices are introduced by a trocar via two small perineal incisions and are placed under fluoroscopic guidance on each side of the bladder neck, close to the vesico-urethral anastomotic site. The balloons can be filled, and their volume can be adjusted post-operatively using a hypodermic needle injected through the intra-scrotal port.

Efficacy: A SR and meta-analysis of nineteen studies including 1,264 patients reported a 60.2% dry rate, significant reduction in number of pads used per day (-3.1) and greatly improved QoL scores for ProACT® [673]; however, the level of heterogeneity among the included studies was high. A comparison between ATOMS® and ProACT®, showed that the former is associated with higher improvement and satisfaction rates and fewer complications [650]. A quasi-randomised trial comparing ProACT® with bone-anchored male slings found that both resulted in similar improvements in SUI (68% vs. 65%, respectively) [674]. A questionnaire study showed that 50% of patients were still significantly bothered by persistent incontinence following ProACT® [675]. A subgroup analysis of radiotherapy patients reported worst outcomes as compared to patients not receiving radiotherapy (46% vs. 68% success rate) as well as a higher percentage of urethral erosion for ProACT® [676].

Tolerability and safety: The most common intra-operative complication during ProACT® implantation is perforation of the bladder and/or urethra. A meta-analysis estimated a perforation rate of 5.3% [673]. The estimated overall revision rate is 22.2%, and the main causes are erosion (3.8%), device leaking (4.1%) and migration (6.5%) [673]. Other prospective series have shown that adverse events were frequent, leading to an explantation rate of 11-58% [674, 675, 677-679].

Practical Considerations: ProACT® has a satisfactory rate of success and seems to be a reasonable alternative for the treatment of male UI; however, it is associated with high complication rates.

Summary of evidence	**LE**
Primary AUS implantation is effective for cure of SUI in men.	1b
There are conflicting data on whether previous pelvic radiotherapy affects the outcome of AUS implantation.	3
The non-circumferential compression device (ProACT®) is effective for treatment of PPI SUI; however, it is associated with a high failure and complication rate leading to frequent explantation and particularly after pelvic radiation therapy.	2b
The rate of explantation of the AUS due to infection or erosion remains high (up to 24% in some series).	3

Recommendations	**Strength rating**
Offer artificial urinary sphincter (AUS) to men with moderate-to-severe stress urinary incontinence.	Strong
Implantation of AUS or ProACT© for men should only be offered in expert centres.	Weak
Warn men receiving AUS or ProACT© that, although cure can be achieved there is a high risk of complications, mechanical failure, and the need for explantation.	Strong
Do not offer non-circumferential compression device (ProACT©) to men who have had pelvic radiotherapy.	Weak

5.6.6 *Surgical treatment for urgency urinary incontinence*

5.6.6.1 *Bladder wall injection of botulinum Toxin-A*

Mechanism of action: The primary mechanism of action of BoNT-A is through the inhibition of neurotransmitter release from cholinergic neurons [525]. OnabotulinumtoxinA (onabotA; BOTOX®) 100 U is licenced in Europe to treat OAB with persistent or refractory non-neurogenic UUI in adults [680, 681].

Efficacy: An RCT of OAB-wet patients whose symptoms were not adequately managed with anticholinergics and who receive either bladder wall injections of onabotA (100 U) or saline reported a 50% reduction in UUI episodes/day whilst the number of micturitions/day reduced by more than two in patients receiving onabotA [682]. A total of 22.9% of the patients in the onabotA arm were fully dry, vs. 6.5% in the saline arm.

A SR and meta-analysis comparing the efficacy of onabotA, mirabegron and anticholinergics in adults with idiopathic OAB reported that patients who received onabotA (100U) achieved greater reduction in UI episodes, surgery, micturition frequency and the highest odds of achieving dryness as well as > 50% reduction from baseline UI episodes per day [683].

A randomised, placebo-controlled pilot study, assessing the effect of onabotA for the treatment of refractory OAB symptoms after prostatectomy reported significantly improved QoL and ICIQ scores and improvements in daily frequency in patients receiving onabotA compared to placebo [684]. A retrospective trial assessed onabotA efficacy in 65 non-obstructed men with refractory OAB and reported significant improvement in UDI-6 score (-4.2) and IIQ-7 (-6.0) scores, compared to baseline [685].

In a retrospective, single-centre cohort study of onabotA treatment for OAB in 120 patients lead to lower CISC rates in male patients after prior de-obstructive surgery than in surgery-naïve patients (28.6% CISC in the group without prior surgery, 7.5% in the TURP subgroup, and 4.2% in the radical prostatectomy subgroup) [686].

A phase IIIb trial randomised solifenacin-naive patients (10% males) with refractory OAB to onabotA, solifenacin or placebo, and showed that patients receiving onabotA had significantly greater changes in UI episodes (-3.19) compared to solifenacin (-2.6) and placebo (-1.33) [687].

A network meta-analysis (male population range 9.8-40.2%) which compared onabotA to mirabegron demonstrated that onabotA was associated with improved outcomes in frequency episodes per day (-0.43, [-1.22-0.37]) and in UI episodes per day (-0.46, [-1.46-0.53]) [688].

Tolerability and safety: Urinary retention and UTIs are the two most common adverse events after onabotA injection. Other reported adverse events include haematuria, dysuria and post-treatment pain [689]. Compared to mirabegron, onabotA is associated with higher risk for UTI and treatment emergent adverse events [688]. A retrospective analysis compared the use of CISC after onabotA injection, among men who had previous prostatectomy vs. those without prior surgery [686]. A 7.5% catheterisation rate after TURP, 4.2% rate after radical prostatectomy and 28.6% rate in men without prior prostate surgery was reported.

Practical Considerations: BoNT-A injections is a recommended treatment option for men with refractory UUI. Despite the lack of a universally accepted injection protocol, gender specific studies and absence of studies in BPO patients, BoNT-A seems superior to medical therapy. It is associated with, higher UTIs and urinary retention risk coupled with the need for repeated injections. A dedicated series in male population, focused on treatment persistence, has shown a high discontinuation rate [690]. Patients treated for OAB with onabotA treatment that have not undergone prior de-obstruction are more likely to develop retention and subsequent CISC.

Summary of evidence	**LE**
A single treatment session of onabotA (100 U) injected in the bladder wall is more effective than placebo at curing and improving UUI/OAB symptoms and QoL.	1b
There is no evidence that repeated injections of onabotA have reduced efficacy, but discontinuation rates are high.	3
There is an increased risk of retention and UTI with onabotA injections.	2

Recommendations	Strength rating
Offer bladder wall injections of onabotulinumtoxinA (100 U) to patients with overactive bladder/urge urinary incontinence refractory to medical therapy.	Weak
Warn patients of the limited duration of response, risk of urinary tract infection and the possible prolonged need for clean intermittent self-catheterisation (ensure that they are willing and able to do so).	Strong

5.6.6.2 Sacral nerve stimulation (neuromodulation)

Mechanism of action: Sacral nerve stimulation (SNS) delivers low amplitude electrical impulses to the sacral nerve roots via an electrode implanted adjacent to the third sacral nerve root and connected to an attached pulse generator implanted in the buttocks. It works by modulating neural activity thus stabilising bladder electrical activity through an unknown mechanism. It is a two-stage process: in the first stage, a tined lead electrode is placed percutaneously near the S3 root and linked to an external stimulator to assess the response. If symptoms reduced more than 50%, patients are candidates for the second stage which is the full implant.

Efficacy: Several trials assess the clinical effectiveness of SNS. All RCTs suffer from the limitation that patients and assessors cannot be blinded to the treatment allocation since all recruited subjects had to respond to a test phase before randomisation. In addition, the percentage of male population in these trials is around 10%. A meta-analysis compared the effectiveness of SNS to onabotA and reported no significant difference in successfully treated cases at six-month follow-up (RR 0.93; 95% CI: 0.63-1.39) [691].

Tolerability and safety: Main complications after SNS are pain at the implant site (13-42%), lead migration (4.0-21%), leg or back pain (3.0-18%) and wound infection (5.7-6.7%). Surgical revision is required in 29-33% of patients due to device malfunction, battery or device replacement or lead migration [692].

Practical Considerations: Sacral nerve stimulation represents an alternative to onabotA in patients with refractory OAB, as it has been shown good success rates and an acceptable safety profile.

Summary of evidence	LE
Sacral nerve stimulation is effective after failed conservative treatment for OAB/UUI, but no sham controls have been used.	2a

Recommendation	Strength rating
Offer sacral nerve stimulation to patients who have urge urinary incontinence refractory to medical therapy and are willing to undergo surgical treatment.	Weak

5.6.6.3 Cystoplasty/urinary diversion

Mechanism of action: Augmentation cystoplasty involves the interposition of a detubularised segment of bowel into the bivalved bladder wall, aiming to increase bladder capacity and reduce OAB related symptoms. Urinary diversion remains a reconstructive option for patients with intractable UI after multiple pelvic procedures, radiotherapy or pelvic pathology leading to irreversible sphincteric incompetence or fistula formation.

Efficacy: There are no RCTs comparing bladder augmentation to other treatments for patients with refractory OAB/UUI. In a large study with three years follow-up augmentation cystoplasty resulted in a post-operative continence rate of 93% in idiopathic detrusor overactivity patients, 78% in neurogenic overactivity and up to 90% when an AUS was implanted, respectively [693]. The largest case series of bladder augmentation in an idiopathic population included only women [694]. At an average follow up of 75.4 months only 53% were continent and satisfied with the surgery, whereas 25% had occasional leaks and 18% continued to have disabling UUI. A small prospective mixed gender trial reported high patient satisfaction rates with augmentation cystoplasty vs. onabotA therapy [695]. A small study comparing ileal with colonic conduits concluded that there were no differences in the relative risks of UUT infection and uretero-intestinal stenosis [696]. However, there are no studies that have specifically examined these techniques in the treatment of intractable OAB/UUI [696]. Therefore, careful consideration on which operation is undertaken will depend on thorough pre-operative counselling, access to stoma/continence nurses as well as patient factors to allow for fully informed patient choice.

Tolerability and safety: Cystoplasty and urinary diversion are major urologic operations. The early post-operative complications include infection, bowel obstruction, bleeding, and cardiorespiratory complications.

Long-term complications include metabolic disturbances (hyperchloraemic metabolic acidosis), change in bowel habits, increased mucus production, stone formation, bladder perforation and rarely bladder cancer [697]. Following augmentation cystoplasty or diversion, the majority of patients will depend on self-catheterisation for bladder emptying. Patients with urinary conduit will depend on lifelong urine bags.

Practical Considerations: Augmentation cystoplasty and urinary diversion represent realistic treatment options for men with refractory OAB. However, both options involve a major operation, with a non-negligible long-term complication rate and a lifelong reliance on catheterisation or urine bags.

Summary of evidence	LE
There is limited evidence of the effectiveness of augmentation cystoplasty and urinary diversion in treatment of idiopathic OAB.	3
The need to perform CISC following augmentation cystoplasty is high.	3
Augmentation cystoplasty and urinary diversion are associated with high risks of short- and long-term complications.	3
There is no evidence comparing the efficacy or adverse effects of augmentation cystoplasty to urinary diversion.	3

Recommendations	Strength rating
Offer augmentation cystoplasty to patients with overactive bladder (OAB)/urge urinary incontinence (UUI) who have failed all other treatment options and are able and willing to perform self-catheterisation.	Weak
Inform patients undergoing augmentation cystoplasty of the high risk of complications; the risk of having to perform clean intermittent self-catheterisation and the need for life-long surveillance.	Strong
Only offer urinary diversion to patients who have failed less invasive therapies for the treatment of OAB/UUI, who will accept a stoma.	Weak

6. FOLLOW-UP

6.1 Watchful waiting (behavioural)

Patients who elect to pursue a WW policy should be reviewed at six months and then annually, provided there is no deterioration of symptoms or development of absolute indications for surgical treatment. The following are recommended at follow-up visits: history, IPSS, uroflowmetry, and PVR volume.

6.2 Medical treatment

Patients receiving α1-blockers, muscarinic receptor antagonists, beta-3 agonists, PDE5Is or the combination of α1-blockers and 5-ARIs or muscarinic receptor antagonists should be reviewed four to six weeks after drug initiation to determine the treatment response. If patients gain symptomatic relief in the absence of troublesome adverse events, drug therapy may be continued. Patients should be reviewed at six months and then annually, provided there is no deterioration of symptoms or development of absolute indications for surgical treatment. The following are recommended at follow-up visits: history, IPSS, uroflowmetry, and PVR volume. Frequency volume charts or bladder diaries should be used to assess response to treatment for predominant storage symptoms or nocturnal polyuria.

Patients receiving 5-ARIs should be reviewed after twelve weeks and six months to determine their response and adverse events. The following are recommended at follow-up visits: history, IPSS, uroflowmetry and PVR volume. Men taking 5-ARIs should be followed up regularly using serial PSA testing if life expectancy is greater than ten years and if a diagnosis of PCa could alter management. A new baseline PSA should be determined at six months, and any confirmed increase in PSA while on 5-ARIs should be evaluated.

In patients receiving desmopressin, serum sodium concentration should be measured at day three and seven, one month after initiating therapy and periodically during treatment. If serum sodium concentration has remained normal during periodic screening follow-up screening can be carried out every three months subsequently. However, serum sodium concentration should be monitored more frequently in patients ≥ 65 years of age and in patients at increased risk of hyponatremia. The following tests are recommended at follow-up visits: serum-sodium concentration and FVC. The follow-up sequence should be restarted after dose escalation.

6.3 Surgical treatment

After prostate surgery, patients should be reviewed four to six weeks after catheter removal to evaluate treatment response and adverse events. If patients have symptomatic relief and are without adverse events, no further re-assessment is necessary. The following tests are recommended at follow-up visit after four to six weeks: IPSS, uroflowmetry and PVR volume.

Summary of evidence	LE
Follow-up for all conservative, medical, or operative treatment modalities is based on empirical data or theoretical considerations, but not on evidence-based studies.	4

Recommendations	Strength rating
Follow-up all patients who receive conservative, medical, or surgical management.	Weak
Define follow-up intervals and examinations according to the specific treatment.	Weak

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8. CONFLICT OF INTEREST

All members of the EAU Non-neurogenic Male LUTS Guidelines Panel have provided disclosure statements of all relationships that they have that might be perceived as a potential source of a conflict of interest. This information is publically accessible through the European Association of Urology website: http://uroweb.org/guideline. This guidelines document was developed with the financial support of the European Association of Urology. No external sources of funding and support have been involved. The EAU is a non-profit organisation and funding is limited to administrative and travel and meeting expenses. No honoraria or other reimbursements have been provided.

9. CITATION INFORMATION

The format in which to cite the EAU Guidelines will vary depending on the style guide of the journal in which the citation appears. Accordingly, the number of authors or whether, for instance, to include the publisher, location, or an ISBN number may vary.

The compilation of the complete Guidelines should be referenced as:
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References to individual guidelines should be structured in the following way:
Contributors' names. Title of resource. Publication type. ISBN. Publisher and publisher location, year.

NICE National Institute for Health and Care Excellence

NICE guideline

Lower urinary tract symptoms in men: management

Clinical guideline
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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

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This guideline replaces IPG256, IPG15, IPG224, IPG120 and ESNM18.

This guideline is the basis of QS45.

This guideline should be read in conjunction with IPG14 and IPG17.

Overview

This guideline covers managing lower urinary tract symptoms (LUTS) in men over 18. It aims to improve the quality of life for men with LUTS by recommending which assessments they should receive, and when conservative management, drug treatment and surgery can help.

Who is it for?

- Healthcare professionals
- Commissioners and providers
- Men with LUTS and their families or carers

Introduction

Lower urinary tract symptoms (LUTS) comprise storage, voiding and post-micturition symptoms affecting the lower urinary tract. There are many possible causes of LUTS such as abnormalities or abnormal function of the prostate, urethra, bladder or sphincters. In men, the most common cause is benign prostate enlargement (BPE), which obstructs the bladder outlet. BPE happens when the number of cells in the prostate increases, a condition called benign prostatic hyperplasia. Other conditions that can cause LUTS include detrusor muscle weakness or overactivity, prostate inflammation (prostatitis), urinary tract infection, prostate cancer and neurological disease. This guideline will advise on the effective evidence-based management of LUTS in men.

LUTS in men are best categorised into voiding, storage or post-micturition symptoms to help define the source of the problem. Voiding symptoms include weak or intermittent urinary stream, straining, hesitancy, terminal dribbling and incomplete emptying. Storage symptoms include urgency, frequency, urgency incontinence and nocturia. The major post-micturition symptom is post-micturition dribbling, which is common and bothersome. Although LUTS do not usually cause severe illness, they can considerably reduce men's quality of life, and may point to serious pathology of the urogenital tract.

LUTS are a major burden for the ageing male population. Age is an important risk factor for LUTS and the prevalence of LUTS increases as men get older. Bothersome LUTS can occur in up to 30% of men older than 65 years. This is a large group potentially requiring treatment.

Because uncertainty and variation exist in clinical practice, this guideline gives clear recommendations on diagnosing, monitoring and treating LUTS.

The guideline will assume that prescribers will use a medicine's summary of product characteristics to inform decisions made with individual men.

Key priorities for implementation

The following recommendations were identified as priorities for implementation in the 2010 guideline and have not been changed in the 2015 update.

Initial assessment

- At initial assessment, offer men with lower urinary tract symptoms (LUTS) an assessment of their general medical history to identify possible causes of LUTS, and associated comorbidities. Review current medication, including herbal and over-the-counter medicines, to identify drugs that may be contributing to the problem. **[2010]**
- At initial assessment, offer men with LUTS a physical examination guided by urological symptoms and other medical conditions, an examination of the abdomen and external genitalia, and a digital rectal examination. **[2010]**
- At initial assessment, ask men with bothersome LUTS to complete a urinary frequency volume chart. **[2010]**
- Refer men for specialist assessment if they have LUTS complicated by recurrent or persistent urinary tract infection, retention, renal impairment that is suspected to be caused by lower urinary tract dysfunction, or suspected urological cancer. **[2010]**

Conservative management

- Offer men with storage LUTS (particularly urinary incontinence) temporary containment products (for example, pads or collecting devices) to achieve social continence until a diagnosis and management plan have been discussed. **[2010]**
- Offer men with storage LUTS suggestive of overactive bladder supervised bladder training, advice on fluid intake, lifestyle advice and, if needed, containment products. **[2010]**

Surgery for voiding symptoms

- If offering surgery for managing voiding LUTS presumed secondary to benign prostate enlargement (BPE), offer monopolar or bipolar transurethral resection of the prostate (TURP), monopolar transurethral vaporisation of the prostate (TUVP) or holmium laser enucleation of the prostate (HoLEP). Perform HoLEP at a centre specialising in the technique, or with mentorship arrangements in place. **[2010]**

- If offering surgery for managing voiding LUTS presumed secondary to BPE, do not offer minimally invasive treatments (including transurethral needle ablation [TUNA], transurethral microwave thermotherapy [TUMT], high-intensity focused ultrasound [HIFU], transurethral ethanol ablation of the prostate [TEAP] and laser coagulation) as an alternative to TURP, TUVP or HoLEP (see recommendation 1.5.2). **[2010]**

Providing information

- Make sure men with LUTS have access to care that can help with:
  - their emotional and physical conditions **and**
  - relevant physical, emotional, psychological, sexual and social issues. **[2010]**
- Provide men with storage LUTS (particularly incontinence) containment products at point of need, and advice about relevant support groups. **[2010]**

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in NICE's information on making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

The following guidance is based on the best available evidence. The full guideline gives details of the methods and the evidence used to develop the 2010 recommendations. The guideline addendum gives details of the methods and the evidence used to develop the 2015 recommendations.

In this guideline, 'mild' refers to an International Prostate Symptom Score (IPSS) of 0 to 7, 'moderate' refers to an IPSS of 8 to 19 and 'severe' refers to an IPSS of 20 to 35.

1.1 Initial assessment

Initial assessment refers to assessment carried out in any setting by a healthcare professional without specific training in managing lower urinary tract symptoms (LUTS) in men.

1.1.1 At initial assessment, offer men with LUTS an assessment of their general medical history to identify possible causes of LUTS, and associated comorbidities. Review current medication, including herbal and over-the-counter medicines, to identify drugs that may be contributing to the problem. **[2010]**

1.1.2 At initial assessment, offer men with LUTS a physical examination guided by urological symptoms and other medical conditions, an examination of the abdomen and external genitalia, and a digital rectal examination. **[2010]**

1.1.3 At initial assessment, ask men with bothersome LUTS to complete a urinary frequency volume chart. **[2010]**

1.1.4 At initial assessment, offer men with LUTS a urine dipstick test to detect blood, glucose, protein, leucocytes and nitrites. **[2010]**

1.1.5 At initial assessment, offer men with LUTS information, advice and time to decide if they wish to have prostate-specific antigen (PSA) testing if:

- their LUTS are suggestive of bladder outlet obstruction secondary to benign prostate enlargement (BPE) **or**
- their prostate feels abnormal on digital rectal examination **or**
- they are concerned about prostate cancer. **[2010]**

1.1.6 Manage suspected prostate cancer in men with LUTS in line with the NICE guidelines on prostate cancer and suspected cancer. **[2010]**

1.1.7 At initial assessment, offer men with LUTS a serum creatinine test (plus estimated glomerular filtration rate [eGFR] calculation) only if you suspect renal impairment (for example, the man has a palpable bladder, nocturnal enuresis, recurrent urinary tract infections or a history of renal stones). **[2010]**

1.1.8 Do not routinely offer cystoscopy to men with uncomplicated LUTS (that is, without evidence of bladder abnormality) at initial assessment. **[2010]**

1.1.9 Do not routinely offer imaging of the upper urinary tract to men with uncomplicated LUTS at initial assessment. **[2010]**

1.1.10 Do not routinely offer flow-rate measurement to men with LUTS at initial assessment. **[2010]**

1.1.11 Do not routinely offer a post-void residual volume measurement to men with LUTS at initial assessment. **[2010]**

1.1.12 At initial assessment, give reassurance, offer advice on lifestyle interventions (for example, fluid intake) and information on their

condition to men whose LUTS are not bothersome or complicated. Offer review if symptoms change. **[2010]**

1.1.13 Offer men referral for specialist assessment if they have bothersome LUTS that have not responded to conservative management or drug treatment. **[2010]**

1.1.14 Refer men for specialist assessment if they have LUTS complicated by recurrent or persistent urinary tract infection, retention, renal impairment that is suspected to be caused by lower urinary tract dysfunction, or suspected urological cancer. **[2010]**

1.1.15 Offer men considering any treatment for LUTS an assessment of their baseline symptoms with a validated symptom score (for example, the IPSS) to allow assessment of subsequent symptom change. **[2010]**

1.2 Specialist assessment

Specialist assessment refers to assessment carried out in any setting by a healthcare professional with specific training in managing LUTS in men.

1.2.1 Offer men with LUTS having specialist assessment an assessment of their general medical history to identify possible causes of LUTS, and associated comorbidities. Review current medication, including herbal and over-the-counter medicines to identify drugs that may be contributing to the problem. **[2010]**

1.2.2 Offer men with LUTS having specialist assessment a physical examination guided by urological symptoms and other medical conditions, an examination of the abdomen and external genitalia, and a digital rectal examination. **[2010]**

1.2.3 At specialist assessment, ask men with LUTS to complete a urinary frequency volume chart. **[2010]**

1.2.4 At specialist assessment, offer men with LUTS information, advice and time to decide if they wish to have PSA testing if:

- their LUTS are suggestive of bladder outlet obstruction secondary to BPE **or**
- their prostate feels abnormal on digital rectal examination **or**
- they are concerned about prostate cancer. **[2010]**

1.2.5 Offer men with LUTS who are having specialist assessment a measurement of flow rate and post-void residual volume. **[2010]**

1.2.6 Offer cystoscopy to men with LUTS having specialist assessment only when clinically indicated, for example if there is a history of any of the following:

- recurrent infection
- sterile pyuria
- haematuria
- profound symptoms
- pain. **[2010]**

1.2.7 Offer imaging of the upper urinary tract to men with LUTS having specialist assessment only when clinically indicated, for example if there is a history of any of the following:

- chronic retention
- haematuria
- recurrent infection
- sterile pyuria
- profound symptoms
- pain. **[2010]**

1.2.8 Consider offering multichannel cystometry to men with LUTS having specialist assessment if they are considering surgery. **[2010]**

1.2.9 Offer pad tests to men with LUTS having specialist assessment only if

the degree of urinary incontinence needs to be measured. **[2010]**

1.3 Conservative management

1.3.1 Explain to men with post-micturition dribble how to perform urethral milking. **[2010]**

1.3.2 Offer men with storage LUTS (particularly urinary incontinence) temporary containment products (for example, pads or collecting devices) to achieve social continence until a diagnosis and management plan have been discussed. **[2010]**

1.3.3 Offer a choice of containment products to manage storage LUTS (particularly urinary incontinence) based on individual circumstances and in consultation with the man. **[2010]**

1.3.4 Offer men with storage LUTS suggestive of overactive bladder supervised bladder training, advice on fluid intake, lifestyle advice and, if needed, containment products. **[2010]**

1.3.5 Inform men with LUTS and proven bladder outlet obstruction that bladder training is less effective than surgery. **[2010]**

1.3.6 Offer supervised pelvic floor muscle training to men with stress urinary incontinence caused by prostatectomy. Advise them to continue the exercises for at least 3 months before considering other options. **[2010]**

1.3.7 Refer for specialist assessment men with stress urinary incontinence. **[2010]**

1.3.8 Do not offer penile clamps to men with storage LUTS (particularly urinary incontinence). **[2010]**

1.3.9 Offer external collecting devices (for example, sheath appliances, pubic pressure urinals) for managing storage LUTS (particularly urinary incontinence) in men before considering indwelling catheterisation (see recommendation 1.3.11). **[2010]**

1.3.10 Offer intermittent bladder catheterisation before indwelling urethral or suprapubic catheterisation to men with voiding LUTS that cannot be corrected by less invasive measures. **[2010]**

1.3.11 Consider offering long-term indwelling urethral catheterisation to men with LUTS:

- for whom medical management has failed and surgery is not appropriate **and**
- who are unable to manage intermittent self-catheterisation **or**
- with skin wounds, pressure ulcers or irritation that are being contaminated by urine **or**
- who are distressed by bed and clothing changes. **[2010]**

1.3.12 If offering long-term indwelling catheterisation, discuss the practicalities, benefits and risks with the man and, if appropriate, his carer. **[2010]**

1.3.13 Explain to men that indwelling catheters for urgency incontinence may not result in continence or the relief of recurrent infections. **[2010]**

1.3.14 Consider permanent use of containment products for men with storage LUTS (particularly urinary incontinence) only after assessment and exclusion of other methods of management. **[2010]**

1.4 Drug treatment

1.4.1 Offer drug treatment only to men with bothersome LUTS when conservative management options have been unsuccessful or are not appropriate. **[2010]**

1.4.2 Take into account comorbidities and current treatment when offering men drug treatment for LUTS. **[2010]**

1.4.3 Offer an alpha blocker (alfuzosin, doxazosin, tamsulosin or terazosin) to men with moderate to severe LUTS. **[2010]**

1.4.4 Offer an anticholinergic to men to manage the symptoms of overactive

bladder. **[2010]**

1.4.5 Offer a 5-alpha reductase inhibitor to men with LUTS who have prostates estimated to be larger than 30 g or a PSA level greater than 1.4 ng/ml, and who are considered to be at high risk of progression (for example, older men). **[2010]**

1.4.6 Consider offering a combination of an alpha blocker and a 5-alpha reductase inhibitor to men with bothersome moderate to severe LUTS and prostates estimated to be larger than 30 g or a PSA level greater than 1.4 ng/ml. **[2010]**

1.4.7 Consider offering an anticholinergic as well as an alpha blocker to men who still have storage symptoms after treatment with an alpha blocker alone. **[2010]**

1.4.8 Consider offering a late afternoon loop diuretic to men with nocturnal polyuria. **[2010]**

In June 2015, loop diuretics (for example, furosemide) did not have a UK marketing authorisation for this indication. See NICE's information on prescribing medicines.

1.4.9 Consider offering oral desmopressin to men with nocturnal polyuria if other medical causes have been excluded and they have not benefited from other treatments. Measure serum sodium 3 days after the first dose. If serum sodium is reduced to below the normal range, stop desmopressin treatment.

Medical conditions that can cause nocturnal polyuria symptoms include diabetes mellitus, diabetes insipidus, adrenal insufficiency, hypercalcaemia, liver failure, polyuric renal failure, chronic heart failure, obstructive apnoea, dependent oedema, pyelonephritis, chronic venous stasis, sickle cell anaemia. Medications that can cause nocturnal polyuria symptoms include calcium channel blockers, diuretics, and selective serotonin reuptake inhibitors (SSRIs). **[2010]**

In June 2015, desmopressin did not have a UK marketing authorisation

for this indication. See NICE's information on prescribing medicines.

1.4.10 Do not offer phosphodiesterase-5 inhibitors solely for the purpose of treating LUTS in men, except as part of a randomised controlled trial. **[new 2015]**

Review

1.4.11 Discuss active surveillance (reassurance and lifestyle advice without immediate treatment and with regular follow-up) or active intervention (conservative management, drug treatment or surgery) for:

- men with mild or moderate bothersome LUTS
- men whose LUTS fail to respond to drug treatment. **[2010]**

1.4.12 Review men taking drug treatments to assess symptoms, the effect of the drugs on the patient's quality of life and to ask about any adverse effects from treatment. **[2010]**

1.4.13 Review men taking alpha blockers at 4 to 6 weeks and then every 6 to 12 months. **[2010]**

1.4.14 Review men taking 5-alpha reductase inhibitors at 3 to 6 months and then every 6 to 12 months. **[2010]**

1.4.15 Review men taking anticholinergics every 4 to 6 weeks until symptoms are stable, and then every 6 to 12 months. **[2010]**

1.5 Surgery for voiding symptoms

1.5.1 For men with voiding symptoms, offer surgery only if voiding symptoms are severe or if drug treatment and conservative management options have been unsuccessful or are not appropriate. Discuss the alternatives to and outcomes from surgery. **[2010]**

1.5.2 If offering surgery for managing voiding LUTS presumed secondary to BPE, offer monopolar or bipolar transurethral resection of the prostate

(TURP), monopolar transurethral vaporisation of the prostate (TUVP) or holmium laser enucleation of the prostate (HoLEP). Perform HoLEP at a centre specialising in the technique, or with mentorship arrangements in place. **[2010]**

1.5.3 Offer transurethral incision of the prostate (TUIP) as an alternative to other types of surgery (see recommendation 1.5.2) to men with a prostate estimated to be smaller than 30 g. **[2010]**

1.5.4 Only offer open prostatectomy as an alternative to TURP, TUVP or HoLEP (see recommendation 1.5.2) to men with prostates estimated to be larger than 80 g. **[2010]**

1.5.5 If offering surgery for managing voiding LUTS presumed secondary to BPE, do not offer minimally invasive treatments (including transurethral needle ablation [TUNA], transurethral microwave thermotherapy [TUMT], high-intensity focused ultrasound [HIFU], transurethral ethanol ablation of the prostate [TEAP] and laser coagulation) as an alternative to TURP, TUVP or HoLEP (see recommendation 1.5.2). **[2010]**

1.5.6 If offering surgery for managing voiding LUTS presumed secondary to BPE, only consider offering botulinum toxin injection into the prostate as part of a randomised controlled trial. **[2010]**

1.5.7 If offering surgery for managing voiding LUTS presumed secondary to BPE, only consider offering laser vaporisation techniques, bipolar TUVP or monopolar or bipolar transurethral vaporisation resection of the prostate (TUVRP) as part of a randomised controlled trial that compares these techniques with TURP. **[2010]**

1.6 Surgery for storage symptoms

1.6.1 If offering surgery for storage symptoms, consider offering only to men whose storage symptoms have not responded to conservative management and drug treatment. Discuss the alternatives of containment or surgery. Inform men being offered surgery that effectiveness, side effects and long-term risk are uncertain. **[2010]**

1.6.2 If considering offering surgery for storage LUTS, refer men to a urologist to discuss:

- the surgical and non-surgical options appropriate for their circumstances and
- the potential benefits and limitations of each option, particularly long-term results. **[2010]**

1.6.3 Consider offering cystoplasty to manage detrusor overactivity only to men whose symptoms have not responded to conservative management or drug treatment and who are willing and able to self-catheterise. Before offering cystoplasty, discuss serious complications (that is, bowel disturbance, metabolic acidosis, mucus production and/or mucus retention in the bladder, urinary tract infection and urinary retention). **[2010]**

1.6.4 Consider offering bladder wall injection with botulinum toxin to men with detrusor overactivity only if their symptoms have not responded to conservative management and drug treatments and the man is willing and able to self-catheterise. **[2010]**

In June 2015, botulinum toxin A and botulinum toxin B did not have UK marketing authorisations for this indication. See NICE's information on prescribing medicines.

1.6.5 Consider offering implanted sacral nerve stimulation to manage detrusor overactivity only to men whose symptoms have not responded to conservative management and drug treatments. **[2010]**

1.6.6 Do not offer myectomy to men to manage detrusor overactivity. **[2010]**

1.6.7 Consider offering intramural injectables, implanted adjustable compression devices and male slings to manage stress urinary incontinence only as part of a randomised controlled trial. **[2010]**

1.6.8 Consider offering urinary diversion to manage intractable urinary tract symptoms only to men whose symptoms have not responded to conservative management and drug treatments, and if cystoplasty or sacral nerve stimulation are not clinically appropriate or are unacceptable

to the patient. **[2010]**

1.6.9 Consider offering implantation of an artificial sphincter to manage stress urinary incontinence only to men whose symptoms have not responded to conservative management and drug treatments. **[2010]**

1.7 Treating urinary retention

1.7.1 Immediately catheterise men with acute retention. **[2010]**

1.7.2 Offer an alpha blocker to men for managing acute urinary retention before removal of the catheter. **[2010]**

1.7.3 Consider offering self- or carer-administered intermittent urethral catheterisation before offering indwelling catheterisation for men with chronic urinary retention. **[2010]**

1.7.4 Carry out a serum creatinine test and imaging of the upper urinary tract in men with chronic urinary retention (residual volume greater than 1 litre or presence of a palpable or percussable bladder). **[2010]**

1.7.5 Catheterise men who have impaired renal function or hydronephrosis secondary to chronic urinary retention. **[2010]**

1.7.6 Consider offering intermittent or indwelling catheterisation before offering surgery in men with chronic urinary retention. **[2010]**

1.7.7 Consider offering surgery on the bladder outlet without prior catheterisation to men who have chronic urinary retention and other bothersome LUTS but no impairment of renal function or upper renal tract abnormality. **[2010]**

1.7.8 Consider offering intermittent self- or carer-administered catheterisation instead of surgery in men with chronic retention who you suspect have markedly impaired bladder function. **[2010]**

1.7.9 Continue or start long-term catheterisation in men with chronic retention for whom surgery is unsuitable. **[2010]**

1.7.10 Provide active surveillance (post-void residual volume measurement, upper tract imaging and serum creatinine testing) to men with non-bothersome LUTS secondary to chronic retention who have not had their bladder drained. **[2010]**

1.8 Alternative and complementary therapies

1.8.1 Do not offer homeopathy, phytotherapy or acupuncture for treating LUTS in men. **[2010]**

1.9 Providing information

1.9.1 Ensure that, if appropriate, men's carers are informed and involved in managing their LUTS and can give feedback on treatments. **[2010]**

1.9.2 Make sure men with LUTS have access to care that can help with:

- their emotional and physical conditions **and**
- relevant physical, emotional, psychological, sexual and social issues. **[2010]**

1.9.3 Provide men with storage LUTS (particularly incontinence) containment products at point of need, and advice about relevant support groups. **[2010]**

Recommendations for research

The guideline committee has made the following recommendations for research. See the full guideline for the full set of research recommendations.

1 Multichannel cystometry

What is the clinical and cost effectiveness of multichannel cystometry in improving patient-related outcomes in men considering bladder outlet surgery? **[2010]**

Why this is important

This research would clarify whether this test could improve the outcome of surgery. By identifying which patients had bladder outlet obstruction, it could improve the chance of a good outcome from surgery. The study should be a randomised controlled trial comparing multichannel cystometry before surgery with no intervention in men waiting to have bladder outlet surgery.

2 Catheterisation

What are the clinical and cost effectiveness and associated adverse events of intermittent catheterisation compared with indwelling catheterisation (suprapubic or urethral) for men with voiding difficulty and chronic retention of urine? **[2010]**

Why this is important

The number of patients in this group is steadily increasing as the population ages and more radical prostatectomies are carried out. Current practice varies widely across the UK with no established standard of good practice. This research could establish the best approach to management in these men and so bring more effective, patient-focused treatment that is more cost effective. The study should be a randomised controlled trial comparing intermittent catheterisation, indwelling suprapubic and indwelling urethral catheterisation. Outcomes of interest would be quality of life, healthcare resource use and adverse events (including leakage, skin breakdown, infection, erosion and death).

3 Products for men with urinary incontinence

What are the clinical and cost effectiveness and associated adverse events of absorbent pads compared with sheath collectors for men with urinary incontinence? **[2010]**

Why this is important

The number of patients in this group is steadily increasing as more radical prostatectomies are carried out and the population ages. Current practice varies widely across the UK with no established standard of good practice. This research could establish the best approach to continence management in these men and so provide more effective, patient-focused treatment that is more cost effective. In current non-specialist practice, bladder training is often not considered, and adequate diagnosis and hence optimal treatment of bladder dysfunction is often not implemented. Evidence-based guidance on selecting the most suitable containment product and its subsequent management will increase the quality of life of patients, use skilled nurse or carer resources more efficiently and reduce the costs of waste of unsuitable or sub-optimal product use. The study should be a randomised controlled trial reporting symptom severity, quality of life, changes in measured leakage and occurrence of adverse events.

4 Male slings

In men with mild to moderate post-prostatectomy urinary incontinence, what is the clinical and cost effectiveness of a male sling or an implanted adjustable compression device, when assessed by symptom severity, quality of life, changes in measured leakage and occurrence of adverse events? **[2010]**

Why this is important

Guidance is needed on the most suitable surgical options for this growing group of men who, until recently, have had no acceptable treatment option other than insertion of an artificial urinary sphincter. Many men consider insertion of an artificial sphincter to be too invasive and too prone to complication or failure, and therefore depend on containment alone for control of their urinary incontinence. A number of new interventions have been devised but it is uncertain which of these offers the best outcomes. This research could lead to clear recommendations and effective treatment for the majority of these men. A randomised controlled trial is recommended, comparing up to three current interventions:

retrobulbar 'non-compressive' male sling, adjustable compression sling, and implanted adjustable compression device.

5 Phosphodiesterase-5 inhibitors

As part of the 2015 update, the committee made an additional research recommendation on treating lower urinary tract symptoms (LUTS) in men.

What is the clinical and cost effectiveness of phosphodiesterase-5 inhibitors (PDE5Is) for treating lower urinary tract symptoms in men who do not have erectile dysfunction? **[new 2015]**

Why this is important

There is a gap in the evidence about the effectiveness of PDE5Is in men with LUTS who do not have erectile dysfunction. The current evidence includes men with LUTS and erectile dysfunction. Therefore, the standing committee decided that it was not appropriate to make a recommendation about the routine use of PDE5Is in clinical practice. More evidence is needed to enable a recommendation to be made on the use of PDE5Is in all men with LUTS, including those without erectile dysfunction. The study should be a randomised controlled trial comparing PDE5Is with usual care in men over 45 years with LUTS without erectile dysfunction. Outcomes should include the International Prostate Symptom Score (IPSS) symptom score, IPSS quality of life, maximal urinary flow, residual urine volume, postural hypotension, headaches and withdrawals due to adverse events.

See the addendum for more information.

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the NICE topic page on lower urinary tract symptoms.

For full details of the evidence and the guideline committee's discussions, see the full guideline. You can also find information about how the guideline was developed, including details of the committee.

NICE has produced tools and resources to help you put this guideline into practice. For general help and advice on putting our guidelines into practice, see resources to help you put NICE guidance into practice.

Update information

June 2015: A recommendation on phosphodiesterase-5 inhibitors has been added to section 1.4 on drug treatment. A research recommendation on phosphodiesterase-5 inhibitors has been added to section 2.5. The addendum contains details of the methods and evidence used to develop these recommendations.

Recommendations are marked as **[new 2015]** or **[2010]**:

- **[new 2015]** indicates that the evidence has been reviewed and the recommendation has been added or updated.
- **[2010]** indicates that the evidence has not been reviewed since 2010.

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Accreditation

Stinson, Emma M

From: Corrigan, Martina <Personal Information redacted by the USI>
Sent: 23 November 2015 08:44
To: Beattie, Caroline
Cc: Glackin, Anthony; Haynes, Mark; O'Brien, Aidan; ODonoghue, JohnP; Suresh, Ram; Young, Michael
Subject: FW: **URGENT** FINAL DRAFT ACTION PLAN FOR COMMENT - Trust action plan and compliance against regional policy for the surgical management of endoscopic tissue resection
Attachments: HSS MD 14 2015 - POLICY ON THE SURGIVAL MANAGEMENT OF ENDOSCOPIC TISSUE RESECTION (2).pdf; REVISED Policy on surgery for endoscopic tissue resection V0 5 after PHA comments.pdf; Letter to Trusts Surgical Policy 17 Sept 15.doc; Trust Action Plan against the Surgical Management of Endoscopic Tissue Resection recomms - 191115 - FINAL DRAFT.docx

Importance: High

Caroline,

I am happy from my perspective that the changes we discussed on Thursday have been included.

I have copied the Urology Consultant Team into this in case they have anything further to add..

Martina

Martina Corrigan
Head of ENT, Urology and Outpatients
Southern Health and Social Care Trust
Craigavon Area Hospital

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From: Beattie, Caroline
Sent: 19 November 2015 21:47
To: Corrigan, Martina; Young, Michael; McGeough, Mary; Kelly, Brigeen; Clarke, Wendy; McCracken, Geoff; Wright, Richard
Cc: Trouton, Heather; Mackle, Eamon; McVey, Anne; Hogan, Martina; Carroll, Ronan; McAllister, Charlie; Quinn, AnneM
Subject: **URGENT** FINAL DRAFT ACTION PLAN FOR COMMENT - Trust action plan and compliance against regional policy for the surgical management of endoscopic tissue resection
Importance: High

Dear All

Thank you for all your help in developing this composite action plan that outlines the Trust's compliance position against each of the 12 recommendations outlined within the newly endorsed regional policy for the surgical management of endoscopic tissue resection. To achieve this outcome there has been significant and collaborative discussion within each of the specialist clinical teams.

The action plan now needs to be approved by Esther Gishkori prior to issue to Dr Little, Assistant Director of Service Development & Screening at the PHA – the deadline for this submission is now ***Monday 23 November 2015***.

Prior to this information being sent to Esther, I would be grateful if you could review the content of this action plan that is pertinent to your division and confirm if you are happy for it to be sent to Esther for its final review and approval. Given the tight deadlines for this work, I would be grateful if you review and provide any comments by close of play tomorrow.

Kind Regards
Caroline

Caroline Beattie
Patient Safety & Quality Manager – Acute Services

Ground Floor Trust Headquarters
Craigavon Area Hospital
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Click on the link to access the Acute Services Page

From the Deputy Chief Medical Officer
Dr Paddy Woods

HSS(MD)14 /2015

Department of
Health, Social Services and Public Safety
www.dhsspsni.gov.uk

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BT4 3SQ

Tel: Personal Information redacted by the USI
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Your Ref:
Our Ref: HSS(MD)14 /2015
Date: 18 August 2015

For Action:

Chief Executives HSC Trusts
Chief Executive HSCB
Chief Executive PHA
Chief Executive RQIA *(for dissemination to independent sector organisations)*

Dear Colleague

POLICY ON THE SURGICAL MANAGEMENT OF ENDOSCOPIC TISSUE RESECTION

ACTION REQUIRED

1. HSC Trusts and independent providers should process this regional policy template for endorsement by the organisational board, or equivalent;

2. HSC Trusts and independent providers should develop action plans to implement the various elements of the endorsed policy;

3. HSC Trusts should work with commissioners to address resource issues arising from these implementation plans in a phased, consistent and timely manner; and

4. the Public Health Agency should report on progress by 30 November 2015.

As a result of the verdict of the Coroner into the cause of death of Mrs Lynn Lewis in October 2013, work was commissioned on ensuring the safe and effective management of procedures involving the use of distending fluids in endoscopic procedures. In recognition of the limited guidance available on the management of these procedures, local work was commissioned, led by Dr Julian Johnston, Assistant Medical Director in Belfast Health and Social Care Trust.

The attached outline policy is the product of that work and we are now commending it for regional implementation.

The policy covers relevant issues including:

- appropriate preparation of patients prior to operation;
- selection of equipment and associated distending medium;
- precautionary measures associated with the distending medium selected;
- necessary measurements prior to, during and after these procedures;
- a good theatre environment in terms of team dynamics; and
- use of the WHO surgical checklist.

We believe this policy covers all aspects of concern raised by the Coroner in light of his findings in this tragic case.

We welcome your full assistance in this matter.

Yours sincerely

Dr Paddy Woods
Deputy Chief Medical Officer

Mrs Charlotte McArdle
Chief Nursing Officer

Cc HSC Trust Medical Directors
HSC Directors of Nursing Services
Chief Executive, BSO
Executive Medical Director/Director of Public Health PHA/HSCB
Dean Medical Faculty, QUB
Dean of Life and Health Sciences, UU
Chief Executive NIPEC
Chief Executive NIMDTA
Director of Safety Forum

This letter is available on the DHSSPS website at
www.dhsspsni.gov.uk/index/phealth/professional/cmo_communications.htm

Insert Trust LOGO	Reference No:

SAMPLE POLICY

Title:	Policy on the surgical management of endoscopic tissue resection, for example during urological, gynaecological and other relevant surgery.			
Author(s)	List name and titles of lead and additional author(s) or group responsible for drafting policy Include contact details			
Ownership:	Insert name of Director / service area / group / directorate			
Approval by:	Insert name of Trust committee / group responsible for approval		**Approval date:**	Insert date each committee approved
Operational Date:	May 2015		**Next Review:**	May 2017
Version No.	V0.5	**Supercedes**	Any legacy policies.	
Key words:	Endoscopic, Resection, Prostatectomy, Myomectomy, TUR syndrome			
Links to other policies				

Date	Version	Author	Comments
20/11/2013	0.1	SE Trust	Initial Draft
03/12/2013	0.2	JR Johnston	Amalgamation of protocols from 5 Trusts.
01/02/2015	0.3	JRJ	Following 3/11/14, 19/01/2015 MLF meetings
20/03/2015	0.4	JRJ	Following regional feedback, NICE publication
August 2015	0.5	PHA	Review by PHA

Recommendations

This policy is part of a region-wide 'collegiate' improvement programme for surgical endoscopic tissue resection, including:

- a plan to use the safest resection technique currently available and its attendant irrigation fluid.
- establishing a set of safe practice standards and precautions to minimise the risk of intravascular absorption.

1. Preoperative workup **must** be geared towards prevention of the TUR syndrome.
2. Introduce Bipolar resection equipment. During the switchover to bipolar equipment, limit the use of glycine following careful risk assessment of individual patients. If glycine is still being used, strictly monitor as detailed in recommendation 5.
3. Engineer changes in the type of procedures performed.
    a. More secondary procedures for management of heavy menstrual bleeding as per NICE recommendations.
4. Increase vigilance when significant haemorrhage is a feature.
5. If continue to use glycine, the following **must** be used.
    a. Measure point-of-care testing (POCT) serum sodium,
        i. preoperatively.
        ii. if the surgery is longer than 30 minutes as a routine.
        iii. intermittently throughout the surgery.
        iv. if there is a 1000 ml fluid deficit.
    b. Dedicated staff for transporting specimens and results.
    c. Surgery, including TURP, TCRE & TCRF must be performed in a 'main' theatre where POCT equipment is immediately available.
    d. Accurate fluid input & output measurement and deficit calculation.
6. For both mono- and bi-polar techniques, limit the distension pressure by,
    a. maintaining it below the mean arterial pressure (MAP).

    and with continuous-flow gravity systems,
    b. limit the height of the irrigating solution container to 60 cm above the patient and certainly never above 100cm;
    c. theatre teams must have a procedure for checking and maintaining an agreed height;
    d. not applying pressure bags to the irrigation fluid bag.
7. Investigate instilling irrigation fluid by using a pressure controlled pump device and purchasing flow/pressure controllers.
8. The theatre team **must,**
    a. be aware of the distending fluid input & output and deficit;
    b. contain a dedicated nurse for fluid balance and deficit calculation, who remains in theatre for the duration of the procedure.
9. If continue to use glycine, the following **must** be used, throughout the procedure,
    a. accurate irrigation fluid input & output measurement and deficit calculation.
10. Preoperatively, for each individual patient, there **must** be an agreed maximum fluid deficit threshold for action. The surgeon and anaesthetist **must** be informed by the nurse when the threshold is reached.
11. Operations should, if possible, not last longer than 60 minutes,
    a. Theatre teams **must** have an established mechanism for measuring time and procedures for alerting surgeon and anaesthetist.
12. Completion of the standard WHO surgical checklist **must** be adhered to. Adoption of a modified WHO checklist for this kind of procedure should be investigated and piloted.

1.0 INTRODUCTION / PURPOSE OF POLICY

1.1 Background

Some endoscopic surgical procedures require the use of an irrigating fluid to distend the operating field to enable a suitable field of vision and to wash away debris and blood. This includes operations such as,

- resection of prostate (TURP) and bladder tumours (TURBT);
- transcervical resection of endometrium (TCRE), transcervical resection of fibroids (TCRF);
- removal of uterine septum, polyps, endometrial ablations;
- cystoscopy, arthroscopy, rectal tumour surgery, vesical ultrasonic lithotripsy and percutaneous nephrolithotripsy.

Endoscopic operations where there is tissue resection can lead to serious complications such as haemorrhage, fluid overload, hyponatraemia, cerebral oedema and death. This policy concentrates on a subset of these, the transurethral resection (TUR) syndrome[1], when systemic intravascular absorption of irrigation fluid can cause serious symptoms.

This policy sets out the steps needed to improve the safety profile of this type of surgery. Using national policies, guidelines and evidence identified in section 7 along with on-going work within the province, its aim is to establish a regional 'collegiate' improvement strategy for all surgical (urology, gynaecology) teams in NI practicing this type of surgery to,

- use the safest resection technique with its attendant irrigation fluid;
- agree a programme of change for the cessation of glycine use;
- develop or adopt techniques that do not rely on glycine as an irrigant;
- use equipment designed to control or reduce vesical or uterine pressure;
- establish a set of safe practice standards and precautions to minimise the risk of intravascular absorption.

Some of the recommendations can be instituted now and some will depend on purchase of equipment.

1.2 Irrigation fluids used

The irrigation fluid used for these electrosurgical procedures should,

- have neutral visual density so that the surgeon's view is not distorted;
- be non-haemolytic and will not lead to haemolysis if it enters the circulation.

Until relatively recently, the standard equipment used to resect tissue was of a **monopolar electrode** design which requires an electrically nonconductive irrigating fluid so the electrical current is not dissipated and can remain concentrated at the cutting point. As described below, use of this type of fluid bears the risk of the TUR syndrome.

Recently introduced **bipolar resection equipment** is different to the monopolar type in that it incorporates both active and return poles on the same electrode. This allows a conductive fluid medium (normal saline) to be

used for the irrigating fluid instead of a 'conventional' nonconductive irrigation fluid (glycine, sorbitol or mannitol).

Irrigating fluids
In the past, **sterile water** was used as the irrigant but was associated with significant morbidity because of water intoxication and intravascular haemolysis.

Modern non-electrolytic solutions containing glycine 1.5%, mannitol or sorbitol are optically clear and were introduced to prevent haemolysis, without dispersing the electric current used for cutting with the resectoscope. Their use in irrigation solutions has reduced the occurrence of significant haemolysis and death.

The most commonly used irrigation fluid has been 1.5 % **glycine solution,** a non-essential amino acid with a low cost and lack of allergic reactions**.** However, it has an osmolality of 200 $mOsm.kg^{-1}$ which is much lower than that of blood [Plasma = 290 $mosmol.kg^{-1}$] and large amounts of this hypotonic irrigation fluid, required to facilitate the procedure, may be absorbed systemically through a vascular bed[2]. This may cause several serious complications known as the **TUR syndrome** which can occur in a variety of surgical disciplines.

Normal saline is used for irrigation with the bipolar resectoscope. It is associated with fewer unfavorable changes in serum sodium and osmolality than is the case when electrolyte-free media are used with monopolar systems[3] e.g. glycine. Its use, however, does not eliminate the need to prevent excess absorption or to closely monitor fluid balance, as overload can occur. Pulmonary oedema is a reported consequence.

1.3 TUR syndrome[4]

The transurethral resection (TUR) syndrome is an iatrogenic form of acute water intoxication from a combination of fluid overload and hyponatraemia. While first recognised in urology, hence its name, it can occur in other surgical specialties e.g. gynaecology.

It is manifested mainly through a classic triad of,

- fluid overload - acute changes in intravascular volume leading to circulatory overload, pulmonary oedema, cardiac failure and even cardiac arrest;
- dilutional hyponatraemia causing central nervous system (CNS) effects such as cerebral edema leading to agitation, confusion, convulsions and coma;
- direct toxicity and metabolism of glycine which may also cause CNS symptoms, most commonly transient blindness and CNS depression, as it is an inhibitory neurotransmitter. Its metabolism yields water (worsening fluid overload) and ammonia.

The incidence of TUR syndrome for TURP appears to have reduced over the last two decades with recent studies demonstrating incidence rates of 0.8% -

1.4%. The occurrence of the TUR syndrome following bladder tumour resection (TURBT) is thought to be rarer but can occur, probably via either an intraperitoneal or extraperitoneal bladder perforation.

There is a observation that the incidence and effects of this syndrome are more pronounced in gynaecological than in urological surgery. Fluid absorption is slightly more common during TCRE than during TURP, with transcervical resection of fibroids (TCRF) being at a further increased risk over TCRE. Whereas hyponatraemia occurs with equal frequency in men and women, it is more likely to produce severe complications in premenopausal women[3]. Nevertheless, the necessity to constantly seek best and safest practice and to encourage change and improvement is the same for both specialties.

1.4 Purpose

This policy outlines a set of principles designed to reduce the development of the TUR syndrome.

1.5 Objectives

To reduce the likelihood of developing the TUR syndrome through,

- correct patient selection and preoperative preparation;
- selection of an appropriate surgical technique;
- electing to use surgical equipment which allows the use of irrigation fluid which will not give rise to the TUR syndrome;
- the application of monitoring aimed at detecting the early warning signs of the TUR syndrome;
- establishing a theatre regime based on good theatre practice principles aimed at reducing the development of the TUR syndrome.

2.0 SCOPE OF THE POLICY

This policy applies to all staff who may be involved in the care of a patient in theatre who receives irrigating fluid into the bladder or uterus or any other organ where significant fluid absorption is a realistic possibility.

It applies to medical staff, nursing staff, midwives, operating department practitioners, technical staff, physicians' assistants (anaesthesia) and other theatre healthcare workers.

This policy does not cover the methods of treatment of the TUR syndrome.

3.0 ROLES/RESPONSIBILITIES

Medical staff to,

- ensure they are fully cognisant of the risks of the TUR syndrome;
- undertake careful consideration of the therapeutic choices when planning the service for endoscopic resection in order to reduce the likelihood of the development of the TUR syndrome.

Management – actively supporting the introduction of therapeutic modalities that aim to reduce the incidence of the TUR syndrome.

All staff involved in the care of the patient, especially in theatre, are responsible for implementing and adhering to the policy principles.

Each ward/theatre sister/charge nurse/clinician involved with this kind of surgery is responsible for ensuring staff comply with this policy and all relevant staff have the responsibility to ensure that they read and comply with the policy contents.

In the event of an untoward incident an adverse incident form must be completed by either the medical officer or nurse in charge of the patient's care.

4.0 POLICY PRINCIPLES

4.1 Definitions

Osmolality: The concentration of osmotically active particles in a solution.

Hypertonic: Higher osmolality (concentration of particles) than that found in normal cells.

Hypotonic (or hypo-osmolar): Lower osmolality (concentration of particles) than that is found in normal cells.

Hyponatraemia: Lower sodium concentration than normally found in plasma.

Resectoscope: An endoluminal surgical device comprising an endoscope (hysteroscope or cystoscope), sheaths for inflow and outflow, and an ''element'' that interfaces a specially designed electrode (or pair of electrodes) with a radiofrequency (RF) electrosurgical generator which can be either monopolar or bipolar.

4.2 Policy Principles

An irrigating fluid is most frequently absorbed directly into the vascular system when a vein has been severed by electrosurgery. The driving force is the fluid pressure; the volume of fluid absorbed depending on the,

- duration of the procedure and resection time;
- degree of opening of blood vessels during surgery;
    - vascularity of the diseased prostate, uterus, fibroid;
    - surgical disruption of the bladder, uterine vessels;
    - capsular or uterine wall perforation or apparent damage to a venous sinus;
- pressure of the distending fluid within the bladder or uterus;
    - height of the irrigation fluid bag above the patient;
    - distension pressure applied to the irrigation fluid.

For safe endoscopic resection using irrigation fluid, consideration of the following topics needs covered,

a. Preoperative workup;
b. Selection of surgical technique;
c. Identification, control and management of haemorrhage;

d. Control of the absorption of irrigation fluid;
    a. Dilutional Hyponatraemia;
    b. Fluid overload;
    c. Glycine toxicity;
e. Theatre environment;
    a. Decision making processes;
    b. Team dynamics;
    c. Knowledge of potential complications.

4.2.1 Preoperative workup

Careful preoperative workup of the patient must include, for example,

- a robust consent process leading to a truly informed patient aware of the hazards of endoscopic resection using irrigation fluids;
- a thorough physiological assessment with attention paid to risk factors such as hypertension, ischaemic heart disease, cardiac failure, anaemia;
- standard haematology and electrolyte analysis - to include a recent haemoglobin, serum sodium;
- careful consideration regarding blood grouping and cross-matching;
- recent investigations aimed at establishing the pathological anatomy and degree of surgical risk especially haemorrhage e.g. ultrasound scan;
- the ready availability of reports of such investigations before surgery commences.

Recommendation 1
Preoperative workup **must** be geared towards prevention of the TUR syndrome.

Urology

These procedures are carried out on a predominantly elderly population with a high incidence of coexisting disease. BPH affects 50% of males at 60 years and 90% of 85-year-olds and so TURP is most commonly performed on elderly patients, a population group with a high incidence of cardiac, respiratory and renal disease.

Gynaecology

Consideration should be given to the timely commencement of any adjuvant therapy prior to the surgery[3], especially if it helps to reduce the risk of haemorrhage and/or causes a reduction in tumour size.

4.2.2 Selection of surgical technique

Urology

Absorption in excess of 1 litre of glycine solution, which is associated with a statistically increased risk of symptoms, has been reported in 5–20% of the TURPs performed[1].

One of the most important recent improvements in this field has been the introduction of bipolar electrode technology (B-TURP). This addresses the

fundamental flaw of monopolar equipment (M-TURP) by allowing resection in a normal saline irrigation. Therefore, the adoption of bipolar TURP/TURBT allows NS irrigation and permits the removal of glycine and its inherent risks from theatre. The risks of the hyponatraemic and hypo-osmolar aspects of the TUR syndrome are eliminated.

There are several manufacturers who have developed bipolar endoscopy systems. Early local adopters of this type of equipment have experience of several of them and have observed a progressive and continuing development cycle which has now resulted in really excellent systems. They also observe that some other manufacturers have not kept pace. It is important that views on the performance of these bipolar systems are based on the most modern examples and on those manufacturers who have managed to develop the most efficient systems.

B-TURP is the most widely and thoroughly investigated alternative to M-TURP[5]. There is now increasing recent evidence[6 - 9] for the effectiveness of bipolar systems as their technical performance has been developed and improved. Indeed there is some evidence[9] that bipolar may be better at improving urine flow rates and also reducing bleeding related complications as well as eradicating the TUR syndrome. With reduced bleeding and improved visibility, resection time can be decreased.

Moreover, recent systematic reviews[7, 9] are not only repeatedly describing equal effectiveness between monopolar and bipolar techniques but are also pointing out the significantly improved safety profile for bipolar.

Significantly, the TUR syndrome has not been reported with bipolar equipment[5]. A recent systematic review and meta-analysis[9] comparing traditional monopolar TURP with bipolar TURP established in 22 trials that the TUR syndrome was reported in 35/1375 patients undergoing M-TURP and in none of the 1401 patients undergoing B-TURP. Even taking into account that one study alone was responsible for 17 of the 35 cases, the accompanying editorial states, "*the elimination of TUR syndrome alone has been a worthy consequence of adopting bipolar technology."*

This is supported by recommendations within the European Association of Urology guidelines[5] on TURP management of April 2014. "*B-TURP has a more favourable peri-operative safety profile compared with M-TURP."*

In 2012, NICE recommended[10] that bipolar techniques are associated with lower rates of complications and in October 2014 they opened up support[11] for the use of transurethral resection in saline which eliminates the TUR syndrome and may also reduce length of stay as well as having cost benefits.

In February 2015, they published their medical technology guidance[12] on a transurethral resection in saline system. They point out that the case for adopting the transurethral resection in saline (TURis) system for resection of the prostate is supported by the evidence.

They also indicate that,

- the TURis system can be used instead of a surgical system called 'monopolar transurethral resection of the prostate' (or monopolar TURP);
- Healthcare teams may want to use the TURis system instead of monopolar TURP because,
    - there is no risk of a rare complication called transurethral resection syndrome;
    - it is less likely that a blood transfusion after surgery will be needed.

NICE used an External Assessment Centre to analyse the clinical evidence and concluded that their meta-analysis found a statistically significant effect in favour of TURis: relative risk 0.18 (95% CI 0.05 to 0.62, p=0.006), corresponding to a number needed to treat to prevent 1 case of TUR syndrome compared with monopolar TURP of 50 patients.

The External Assessment Centre did not identify any special additional training needs for a switch to the TURis system from monopolar transurethral resection of the prostate (TURP). The NICE Committee received expert advice that confirmed that little training is needed for surgeons who are already performing monopolar TURP procedures.

The sources of evidence considered by the NICE committee included expert personal views from at least 5 clinical experts from the British Association of Urological Surgeons (BAUS).

NICE, in February 2015, also issued guidance for the public on this topic. They indicated that, "*the TURis system can be used instead of a surgical system called 'monopolar transurethral resection of the prostate'. Healthcare teams may want to use the TURis system instead of monopolar TURP because there is no risk of a rare complication called transurethral resection syndrome and it is less likely that a blood transfusion after surgery will be needed."*

Therefore, the case for moving from a monopolar to bipolar technique for resection of the prostate would appear to be well established as safer with regard to the development of the TUR syndrome. However, it should be remembered that the use of NS is not without risk because there will still be fluid absorption with plasma volume expansion.

Also, queries have been expressed over a potential degradation of pathological specimens with the use of this new technology which might have staging implications for bladder tumour management. However, the experience of both surgical and pathology staff within the BHSCT has been that they have not noticed any major difference. There is also no evidence based literature to support the view that bipolar resection causes any more damage and in fact the incidence of severe cautery artefact was significantly lower in the bipolar resections[13], a view subsequently supported in an accompanying editorial[14] which also exhorts, "*as urologists we have shown again and again that we are quick to adopt new technologies in routine practice*".

Therefore (as long as they are proven to be safe and effective as judged by the NICE interventional procedure programme), bipolar RF systems and other techniques e.g. laser systems, should be introduced regionally. By introducing the, as effective, but safer bipolar equipment, this should, by necessity, reduce and curtail the use of glycine as an irrigation fluid. Its continuing use should be strictly monitored and eventually terminated when there ceases to be circumstances when its use is considered the safest.

Recommendation 2
Introduce Bipolar resection equipment. During the switchover to bipolar equipment, limit the use of glycine following careful risk assessment of individual patients. If glycine is still being used, strictly monitor as detailed in recommendation 5.

Gynaecology
The first generation endometrial ablative techniques including transcervical resection of endometrium (TCRE) and rollerball endometrial ablation (REA) are all endoscopic procedures. Fluid absorption is slightly more common during TCRE than during TURP, with transcervical resection of fibroids (TCRF) being at a further increased risk over TCRE. As TCRE often evolves into a TCRF when fibroids are found during hysteroscopy, it means the same safety procedures need to be put into place for both TCRE and TCRF.

Their effectiveness in the management of heavy menstrual bleeding (in comparison with hysterectomy - the existing gold standard) has been demonstrated in a number of randomised controlled trials. Although less morbid than hysterectomy, they are associated with a number of complications including uterine perforation, cervical laceration, false passage creation, haemorrhage, sepsis and bowel injury and, importantly, the fluid overload and hyponatraemia associated with the use of 1.5% glycine irrigation fluid resulting in the serious and occasionally fatal consequences discussed above.

However, there are now second generation ablative techniques which do not require the use of electrocautery or the use of glycine or other distension fluids. They avoid the serious risk of hyponatraemia and represent simpler, quicker and potentially more efficient means of treating menorrhagia.

A Cochrane Collaboration review (2013)[15] concludes that "*Overall, the existing evidence suggests that success, satisfaction rates and complication profiles of newer techniques of ablation compare favourably with hysteroscopic techniques.*"

NICE[16] in their online guidance for Heavy Menstrual Bleeding recommend,

- First-generation ablation techniques (e.g. rollerball endometrial ablation [REA] and TCRE) are appropriate if hysteroscopic myomectomy (TCRF) is to be included in the procedure;

- All women considering endometrial ablation should have access to a second-generation ablation technique.

Recommendation 3
Engineer changes in the type of procedures performed. • More secondary procedures for management of heavy menstrual bleeding as per NICE recommendations.

If hysteroscopic procedures such as TCRE and TCRF are considered to be the best options and a distending fluid is required, the choice of fluid then comes under the same scrutiny as above for Urology. The choice of using a monopolar scope system using glycine versus bipolar equipment using saline becomes the choice. Evidence is now emerging from gynaecology units in Northern Ireland that are measuring the serum sodium intraoperatively during every case, that there can be concerning incidences of acute hyponatraemia when glycine is used as the distending agent during TCRE[17]. With the development of newer bipolar systems it is recommended that saline has a better safety profile[3].

Therefore, this policy recommends that, (as long as they are proven to be safe and effective as judged by the NICE interventional procedure programme,) the use of second generation ablative techniques and bipolar RF systems should be introduced regionally and the use of glycine as a irrigant curtailed, strictly monitored when it is still used and eventually terminated when there ceases to be circumstances when its use is considered the safest.

4.2.3 Identification, control and management of haemorrhage.

Blood loss can be difficult to quantify and may be significant. Close attention to the patient's clinical state and good communication between surgeon, anaesthetist and the theatre team is vital.

Because of the generalised physiological effects of haemorrhage and the increased likelihood of fluid absorption when using irrigation fluid in the presence of 'open' vasculature, the presence of significant bleeding should act as a trigger for,

- increased vigilance for development of fluid overload, hyponatraemia;
- additional help from medical and nursing staff to assist by scrubbing in;
- increased frequency of haemoglobin and/or haematocrit measurements;
- preparation of blood for cross matching;
- control of the bleeding which may need cessation of the operation.

Recommendation 4
Increase vigilance when significant haemorrhage is a feature.

4.2.4 Control of the absorption of irrigation fluid

To control the effects of fluid absorption, the theatre team should pay particular attention to,

a) Hyponatraemia;
b) limiting the volume of fluid absorbed.

a. Hyponatraemia

The uptake of 1000 ml of fluid would generally correspond to an acute decrease in the serum sodium concentration of 5-8 mmol/L.[2] Encephalopathy, seizures and even cerebral oedema may develop when the sodium concentration falls below 120mmol.L^{-1}. However, even markedly hyponatraemia patients may show no signs of water intoxication. The crucial physiological derangement of CNS function is not just hyponatraemia *per se*, but also the presence of acute hypo-osmolality[4].

Also, a patient's serum sodium concentration and osmolality may continue to decrease for some time after the procedure because irrigant can be slowly absorbed from the perivesicular and retroperitoneal spaces. Therefore, the TUR syndrome can start 4 to 24 hours later – postoperatively, in the recovery ward or back in the ward.

Whereas hyponatraemia occurs with equal frequency in men and women, premenopausal women are 25 times more likely to die or have permanent brain damage than men or postmenopausal women, most likely an oestrogen effect[3]. This effect is compounded because fluid absorption is slightly more common during TCRE than during TURP, and especially so with TCFR.

Serum Sodium measurement

Monitoring serum sodium concentration during TURP is common practice and a low value will confirm the diagnosis of hyponatraemia and is effective for assessing intravascular absorption. Significant decreases from a normal preoperative level can occur after just 15 minutes of starting resection. Levels below 120mmol.L^{-1} are invariably symptomatic and a rapid fall is more likely to produce symptoms.

Point-of-care testing (POCT) is defined as medical testing at or near the site of patient care. It brings the test conveniently and immediately to the patient increasing the likelihood that the patient, physician, and care team will receive the results in minutes, enabling diagnosis of hyponatraemia as early as possible and allowing immediate clinical management decisions to be made. They can be used to measure haematocrit, determine haemoglobin and measure serum electrolytes.

Serum sodium is often only measured at the end of surgery but, in the surgical settings pertaining herein, this monitoring technique is best applied before and repeatedly during surgery so that it can act as a warning system for hyponatraemia. Trusts already operating this method of monitoring have uncovered episodes of unsuspected hyponatraemia; highlighting the need to be wary of glycine and to monitor accordingly. Previous audits that have not

measured serum sodium as part of their audit criteria are thus likely to have given a false sense of security when using glycine.

Any patient receiving glycine in theatre **must** have such POCT equipment readily available and a measurement(s) made,

- as a preoperative baseline prior to the start of surgery;
- if the surgery is longer than 30 minutes;
- intermittently throughout a case as a routine;
- if there is a 1000 ml fluid deficit.

Staff must be readily available who are trained to use this POCT equipment and indeed immediately available to transport the samples and result to and from the machine.

NOTE: Measurement of serum sodium is not required when using a bipolar technique and saline[8].

Recommendation 5
If continue to use glycine, the following **must** be used. a. Measure POCT serum sodium, i. preoperatively; ii. if the surgery is longer than 30 minutes as a routine; iii. intermittently throughout the surgery; iv. if there is a 1000 ml fluid deficit. b. Dedicated staff for transporting specimens and results; c. Surgery, including TURP, TCRE & TCRF must be performed in a 'main' theatre where POCT equipment is immediately available; d. Accurate fluid input & output measurement and deficit calculation.

b. <u>Limit the volume of fluid absorbed.</u>

The choice of surgical technique and equipment may reduce the complications from irrigation fluid by limiting the use of glycine but continued attention to controlling fluid absorption will still be needed if normal saline is used as the distending fluid.

Basic principles govern the amount of fluid absorbed[18].

i. The hydrostatic driving pressure of the distending fluid. This is often a feature of the height of the container but the pressure may be controlled mechanically.
ii. Measurement, monitoring and documentation of the fluid volumes and deficits.
iii. The length of the surgical procedure.

i. Hydrostatic driving pressure of the distending fluid

Surgeons have a vital role in minimising absorption by keeping the cavity distention pressure at the lowest pressure necessary to distend, consistent with good visualisation. Even though the disruption in the vascular system is venous, the best strategy is to measure arterial pressures (which is easy to

do) and to maintain distending pressure below the mean arterial pressure (MAP).

It is estimated that approximately 40mmHg distending pressure is required to obtain clear vision. At pressures between 40mmHg and approximately 100mmHg (MAP), blood will continue to escape from disrupted capillaries until it is stopped by the tamponade. At this point, when continuous flow is used through the resectoscope, the blood within the cavity will be removed and a clear field of vision will be maintained. Dropping the pressure permits further bleeding. If the pressure is raised above the MAP, the pressure not only prevents the flow of blood out of disrupted vessels but actually forces the distension fluid medium in the reverse direction into the vessels.

There exist a number of fluid delivery systems, ranging from those based on simple gravity to automated pumps that are designed to maintain a pre-set intra-cavity pressure. Methods of instilling the distention fluid include,

- continuous-flow by gravity;
- continuous-flow infusion pump;
- pressure-controlled or pressure-sensitive fluid pumps.

Continuous-flow by gravity

In continuous-flow gravity systems, pressure is controlled by the height of the fluid source above the bladder or uterus and is measured from the height of the highest portion of the continuous column of fluid (fluid bag) to the level of the uterus or bladder – approximately 30 cms height is equivalent to 25 mm Hg pressure[19]. If the bag is 60 cms above the patient's uterus, this results in approximately 50 mm Hg of pressure.

Height of fluid column	Pressure exerted
12 inches ≡ 30 cms	25 mmHg
24 inches ≡ 60 cms	50 mmHg
36 inches ≡ 90 cms	75 mmHg

Gravity based systems are very simple to assemble and operate, but require vigilant patient monitoring and frequent manual intake/output calculations, which can be imprecise.

Recommendation 6

For both mono- and bi-polar techniques, limit the distension pressure by,

a. maintaining it below the mean arterial pressure (MAP).

and with continuous-flow gravity systems,

b. limit the height of the irrigating solution container to 60 cm above the patient and certainly never above 100cm;
c. theatre teams must have a procedure for checking and maintaining an agreed height;
d. not applying pressure bags to the irrigation fluid bag.

Continuous-flow infusion pump
Continuous-flow fluid infusion pumps provide a constant flow of distention fluid at the in-flow pressure determined by the operator, delivering the same flow rate regardless of the out-flow conditions. Continuous flow pumps do not usually monitor or calculate the intracavity pressure. Significant fluid absorption and complications can occur with these types of systems because the team is unaware of the actual pressure being used during a prolonged or invasive procedure.

Pressure-controlled or pressure-sensitive fluid pumps
Pressure-controlled infusion pumps can be preset to maintain a desired in-flow pressure. By adjusting the in-flow pressure setting on the pump, it can be maintained below the MAP, thus reducing the likelihood of intravasation.

These pumps can weigh the fluid volume before infusion, which allows them to account for the overfill often found in fluid bags. Weight of fluid before installation and then after, accounts for the deficit, which provides a more accurate measurement of the fluid retained by the patient (fluid deficit). A continuous automated weighing system provides an easy, less time-consuming and valid method of monitoring fluid deficit[2] and an automated fluid management system is recommended[3].

Recommendation 7
Investigate instilling irrigation fluid by using a pressure controlled pump device and purchasing flow/pressure controllers.

ii. Measurement, monitoring & documentation of the fluid volumes & deficits.
If continuous irrigation using fluid filled bags and gravity continue to be used, volumetric fluid balance is based on counting the number of empty fluid bags and then subtracting the out-flow volume in the collection canister and fluid in the drapes to determine irrigation fluid deficit. Positive values are regarded as absorption. The surgeon should be notified about ongoing fluid absorption early enough for steps to be taken to prevent excessive absorption.

However[1], calculation of systemic absorption is complicated by 4 factors,
1. It may be difficult to collect all of the media (fluid, urine and blood) that passes out of the operative area, including that which falls on the procedure or operating room floor;
2. the actual volume of media solution in 3L bags is typically more than the labelled volume;
3. difficulties in estimating the volume of media left in a used or ‘emptied’ infusion bag;
4. systemic absorption that in some instances may occur extremely rapidly.

While these factors can make volumetric fluid balance measurement an unreliable tool, it is considered a minimum necessity when using fluid filled bag systems that the whole theatre team are aware of the distending fluid

input & output and the irrigation fluid deficit. This is especially true for cases where glycine is used.

A member of staff must be assigned to this duty before the start of every case. They will need to be proficient and practiced in this technique and must take responsibility for measuring the input and output, calculating the deficit and recording these details. They should remain in theatre for the duration of the procedure, in the same fashion as the surgeon.

Recommendation 8
The theatre team **must**, • be aware of the distending fluid input & output and deficit; • contain a dedicated nurse for fluid balance and deficit calculation, who remains in theatre for the duration of the procedure.

When using a pressure-controlled infusion pump to control the distension fluid with their associated continuous automated weighing system, the monitoring of the fluid deficit is easier[2], less time-consuming and thus an automated fluid management system is recommended[3].

Documentation

Each patient who has any irrigating fluid used must have documentation in the way of a dedicated fluid management chart (appendix 1) commenced. This can be either the measurement of input & outputs and calculating the deficit or recording the readings off an automated machine.

This should be done as a minimum every time a bag (often 3 litre) is hung up and the details clearly expressed verbally to the surgeon and all other theatre staff. These details should be recorded on the dedicated fluid management chart. They might also be displayed on a white marker board in the theatre.

At the end of the procedure, the final calculations or readings must be made; the inputs, outputs and deficit. These should be expressed clearly to the surgeon and anaesthetist and recorded on the chart. The operating surgeon should include the fluid deficit in the *Operative Findings* when writing the operative notes.

The fluid management chart must follow the patient into the recovery ward. All fluid balances must be handed over to recovery ward staff as part of the normal nursing and medical handover. The chart is then to be filed in the clinical record.

Recommendation 9
If continue to use glycine, the following **must** be used, throughout the procedure, • accurate irrigation fluid input & output measurement and deficit calculation.

Maximum fluid deficit

Prevention of the TUR syndrome requires that the team have a protocol for responding to any escalating fluid absorption and there must be agreed volume thresholds for action. These thresholds may necessarily vary depending on the,

- nature of the surgery;;
- nature of the media (isotonic or hypotonic);
- patient's baseline;
- intraoperative medical condition e.g. presence of haemorrhage.

Considering glycine use, a 500 ml threshold may be appropriate for those who are older and/or medically compromised while for healthy individuals absorption of up to 1000 mL can generally be tolerated. Greater than 1000 mL of glycine intravasation results in a significant decrease in serum sodium, sufficient to bring a normo-natraemic patient into the abnormal range[1, 2, 3].

The surgeon and anaesthetist must be informed by the nurse when there is a 1000mls glycine deficit. Surgery must be brought to a close unless continuation of surgery is absolutely necessary to control the haemorrhage. The nurse must ensure that the surgeon and anaesthetist acknowledge that they have received this information. This must be documented in the notes along with any action taken.

Considering normal saline use, the maximum limit is unclear, but 2500 mL has been advocated[3]. Surgery must be brought to a close unless haemorrhage needs controlled.

Recommendation 10
Preoperatively, for each individual patient, there **must** be an agreed maximum fluid deficit threshold for action. The surgeon and anaesthetist **must** be informed by the nurse when the threshold is reached.

iii. The length of the surgical procedure.

Estimates of the amount of fluid absorbed range from 10 – 30 mls per minute of resection time; over a 45 – 60 minute case that could equate to 1 – 1.8 litres.

Procedures that last longer than 60 minutes and those that require large amounts of tissue resection are more likely to lead to fluid volume overload. Theatre teams must have an established mechanism for measuring time and procedures for alerting surgeon and anaesthetist.

Recommendation 11
Operations should, if possible, not last longer than 60 minutes. Theatre teams **must** have an established mechanism for measuring time and procedures for alerting surgeon and anaesthetist.

4.2.5 Theatre environment

A good theatre environment in terms of team dynamics is essential for the safe performance of these surgical procedures. There must be careful monitoring of fluid balance along with the clear communication of that balance to the surgical and anaesthetic members of the team.

- Theatre staff must always be aware of the potential hazards of, and equipment used, for any surgical procedure before it is performed.
- One core member of the theatre team must be assigned to the duty of gathering together the information needed to ensure the whole theatre team are aware of the distending fluid input & output and the deficit. They will need to be proficient and practiced in this technique and must not have other duties to perform while monitoring fluid balance. It would not be expected that the surgeon should have to operate and also supervise this function at the same time. They should remain in theatre for the duration of the procedure, in the same fashion as the surgeon.
- Medical staff must always have situational knowledge of the theatre environment that they are working in and the availability (or non-availability) of any theatre equipment they consider necessary. They must be informed, in good time, of any equipment that is not working.
- Nursing staff should have a working knowledge of any equipment being used in their theatre or have the immediate presence of technical staff who do have that knowledge.

4.2.6 WHO checklist

Completion of the WHO surgical checklist with the sign in, time out and sign out must be adhered to. This will allow a surgical, anaesthetic and theatre team brief at the beginning for the whole theatre team and an opportunity to check that everything is in place to perform the biochemical and volumetric monitoring, to agree fluid absorption volume limits and should include any discussion of limiting intravenous fluids intraoperatively.

It will also ensure at the sign out that any problems e.g. over a fluid deficit, are identified early. On a regional basis, adoption of a modified WHO checklist for this kind of procedure should be investigated and piloted.

Recommendation 12
Completion of the standard WHO surgical checklist **must** be adhered to. Adoption of a modified WHO checklist for this kind of procedure should be investigated and piloted.

5.0 IMPLEMENTATION OF POLICY

This policy, after it is agreed, is to be implemented throughout NI in each of the 5 Trusts.

5.1 Resources

There will be resource implications in terms providing surgical equipment that can be used without needing glycine as an irrigant, fluid flow and pressure controllers and POCT monitoring equipment for theatres and training for staff.

6.0 MONITORING

Trust audit departments will need to monitor that the recommendations are implemented.

7.0 EVIDENCE BASE / REFERENCES

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8.0 CONSULTATION PROCESS

Consulted through the Medical Leaders Forum, DHSSPSNI, and via the Medical Directors, Directors of Nursing and Regional Urologists, Gynaecologists and Anaesthetists.

9.0 APPENDICES / ATTACHMENTS

Appendix 1 = Suggested peri-operative theatre record form template.

10.0 EQUALITY STATEMENT

In line with duties under the equality legislation (Section 75 of the Northern Ireland Act 1998), Targeting Social Need Initiative, Disability discrimination and the Human Rights Act 1998, an initial screening exercise to ascertain if this policy should be subject to a full impact assessment has been carried out. The outcome of the Equality screening for this policy is:

Major impact ☐

Minor impact ☐

No impact. ☐

SIGNATORIES

_____ **Date:** _____

Author

_____ **Date:** _____

Author

_____ **Date:** _____

Director

Insert Trust LOGO

Peri-operative fluid recording chart

Date: _____
Surgeon: _____
Anaesthetist: _____
Team Leader: _____
Circulating Nurse 1: _____
Circulating Nurse 2: _____

Addressograph Label

Fluid recorder: _____ Operation: _____

Fluid Medium: 3L 1.5% Glycine: ☐ 0.9% NaCl: ☐ Warmed: ☐

Bag Height: _____ mmHg ☐ (60 cms ≡ 50mmhg)

Preop. Serum Sodium: = _____ mmol/L Haemoglobin: _____ g/dL.

Resection: Start Time: _____:_____ Operation Finish Time: _____:_____

Irrigation fluid: Start time: _____:_____ **= 0 mins.**

Time (min)	Irrigation In	Irrigation Out	Irrigation Deficit	Running Deficit	Serum Sodium	Surg. informed	Anaes. informed	Sign
5	mls	mls	mls	mls	mmol/L			
10	mls	mls	mls	mls	mmol/L			
15	mls	mls	mls	mls	mmol/L			
20	mls	mls	mls	mls	mmol/L			
25	mls	mls	mls	mls	mmol/L			
30	mls	mls	mls	mls	mmol/L			
35	mls	mls	mls	mls	mmol/L			
40	mls	mls	mls	mls	mmol/L			
45	mls	mls	mls	mls	mmol/L			
50	mls	mls	mls	mls	mmol/L			
55	mls	mls	mls	mls	mmol/L			
60	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			

Total Fluid In =	mls	Surgeon Signature	
Total Fluid Out =	mls	Anaesthetist Signature	
Total Deficit =	mls	Nurse Signature	
		Recovery Staff Signature	

Insert Trust LOGO

Continued.

Time (mins)	Irrigation In	Irrigation Out	Deficit	Running deficit	Serum Sodium	Surg. informed	Anaes. informed	Sign
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			

Irrigation In	Document number of mls after each fluid bag is emptied. Record amount 'in' each time use Ellick evacuator.
Irrigation Out	Record fluid in • suction canisters. • fluid in drapes. • fluid from floor suction. Record amount 'out' each time use Ellick evacuator.
Deficit	Calculate deficit or record from pump readout.
Serum Sodium	Ensure there is a Serum Sodium measurement within one bold bordered box if procedure longer than 30 mins.

Glycine		
Volume Absorbed	**Effect**	**Action**
500 mls	Limit for the Elderly : comorbidities	Continue surgery
less than 1000 mls	Well tolerated by healthy patient	Continue Surgery
greater than 1000 mls	Mild hyponatraemia	Complete surgery ASAP
1500 mls	**Severe hyponatraemia & other biochemical disturbances likely**	**Stop Surgery**
Normal Saline		
2000 mls	Limit in the healthy	Complete surgery ASAP

Public Health Agency

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Belfast
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www.publichealth.hscni.net

HSC Trust Medical Directors:-
Belfast Health and Social Care Trust
South Eastern Health and Social Care Trust
Southern Health and Social Care Trust
Northern Health and Social Care Trust
Western Health and Social Care Trust

17th September 2015

Dear Colleagues

Re: Progress on HSS(MD) 14/2015
Policy on the Surgical Management of Endoscopic Tissue Reaction

The DHSSPS wrote to your Trust (letter attached for ease of reference) requiring that :-

- The Trust should endorse the policy
- The Trust should develop action plans to implement the policy

I would ask that you provide an update on progress within your Trust by 31st October 2015.

This will facilitate progressing any issues which require input from HSCB/PHA and to enable the PHA to report to the DHSSPS by 30th November 2015.

Yours sincerely

Dr Janet Little

Assistant Director of Service Development & Screening

CC Lynn Charlton, Margaret McNally

Improving Your Health and Wellbeing

Southern Health and Social Care Trust

ACTION PLAN

Reference	HSS (MD) 14/2015
Title of Clinical Guideline / Standard	Policy on the surgical management of endoscopic tissue resection, for example during urological, gynaecological and other relevant surgery
Date of Endorsement and Issue from External Agency:	18/08/2015
Submission Date for Assurance Response / Action Plan to HSCB:	31/10/2015 was the initial deadline date Letter from Dr Little (DHSSPSNI) received 03/11/2015 requesting an update Two week extension given – new deadline for submission 23/11/2015
Directorate/s affected by guideline recommendations	Acute Services
Operational Director	Mrs Esther Gishkori
Identified Change Leader	Mrs Mary McGeough – Head of ATICS Mrs Wendy Clarke – Acting Head of Midwifery & Gynaecology Dr G. McCracken – Clinical Director IMWH Mrs Martina Corrigan – Head of ENT and Urology Mr Young – Lead Consultant Urologist

Actions for Trusts					
Recommendation	**Current Control Measures**	**Current level of compliance (%)**	**Action plan**	**Designated Lead**	**Deadline for completion**
1. Preoperative workup **must** be geared towards prevention of the TUR syndrome.	All of these patients are optimised for surgery and as part of the pre-operative work up, the risk factors pertaining to TUR syndrome are identified and managed. Within Urology all patients are provided with a BAUS information Leaflet and at clinic appointment are advised verbally of the risk factors. All patients have standard haematology and electrolyte analysis completed and have careful consideration regarding blood grouping and cross matching.		An audit will be carried out to review the consent process for patients to determine if the patients have been "*truly made aware of the hazards of endoscopic resection using irrigation fluids*". Patients will be identified from Theatre Management System. Recent Investigations aimed at establishment of pathological anatomy and degree of Surgical risk to be scoped Availability of reports of such investigations prior to commencement of surgery to also be scoped	Mrs Mary McGeough (Head of ATICS)	31/12/2015
2. Introduce Bipolar resection equipment. During the switchover to bipolar equipment, limit the use of glycine following careful risk assessment of individual patients. If glycine is still being used, strictly monitor as detailed in recommendation 5.	Within Gynae services bipolar resection equipment is in place within CAH and DHH (with the exception of one Consultant). Glycine is not used at all. The only exception to this is when there is a failure of the bipolar equipment		Ensure robust and monitored control measures are in place for the use of Glycine within urology services	Mrs Mary McGeough (Head of ATICS)	Ongoing

	and there is a need to revert back to the monopolar equipment. In the event of this rare occurrence there is strict monitoring of glycine in compliance with recommendation 5. Within Urology Services a trial of bipolar resection equipment is currently being undertaken by all of the Urology Consultants. Glycine is still in use.		Complete trial of bipolar equipment - There are 4 pieces of equipment being trialled for 6 weeks each to allow the Team to agree which is the most suitable. Commence procurement process if equipment is deemed suitable	Mr Young (Lead Consultant Urologist) Mrs Mary McGeough (Head of ATICS)	31/03/2016 31/03/2016
3. Engineer changes in the type of procedures performed. More secondary procedures for management of heavy menstrual bleeding as per NICE recommendations.	Within gynae secondary procedures are applied but there is skills maintenance of first generation procedures so that the skill base is maintained for abnormal uterine pathology		On-going monitoring and review	All staff working within ATICS, Gynaecology	On-going
4. Increase vigilance when significant haemorrhage is a feature	The need for increased vigilance when significant haemorrhage is a feature is standard practice across all theatre environments. Trust guideline for the management of Blood Loss (2012) is in place and accessible by all staff on the Trust intranet		On-going monitoring and review	All staff working within ATICS, Gynaecology and Urology services	On-going

	Emergency theatre drills carried out on an annual basis and learning from this drill exercise is fed back to the clinical teams and to the Haemovigilence Team for monitoring / action planning				
5. If continue to use glycine, the following **must** be used. a. Measure point-of-care testing (POCT) serum sodium, i. preoperatively. ii. if the surgery is longer than 30 minutes as a routine. iii. intermittently throughout the surgery. iv. if there is a 1000 ml fluid deficit.	Compliant Compliant Compliant Compliant		Ongoing monitoring and review	All staff working within ATICS, Gynaecology	On-going
5b. Dedicated staff for transporting specimens and results.	This recommendation is not complied with. A member of staff who is available when specimens / results from specimens need to be transported will carry out this task. In October 2015 the Trust's Point of Care Committee has just approved the purchase of 5 POCT machines for ATICS – 4 to be used within CAH theatres / DPU and 1 for use within DHH theatres.	N/A	To purchase 5 POCT machines funding of £27k will be required. IPT is currently being completed for review and approval. When the 5 POCT machines are purchased blood results can be obtained within the theatre environment negating the need for a dedicated member of staff to carry out this task	Mrs Mary McGeough Head of ATICS Mr Ronan Carroll AD - CCS	31/03/2016

5c. Surgery, including TURP, TCRE & TCRF must be performed in a 'main' theatre where POCT equipment is immediately available	When the funding is allocated and equipment purchased 1 of the 5 ISTAT machines will be provided to Day Procedure Unit (CAH) to facilitate the carrying out of these surgical procedures		To purchase 5 POCT machines funding of £27k will be required. IPT is currently being completed for review and approval. When the 5 POCT machines are purchased blood results can be obtained within the theatre environment negating the need for a dedicated member of staff to carry out this task	Mrs Mary McGeough Head of ATICS Mr Ronan Carroll AD - CCS	31/03/2016
5d. Accurate fluid input & output measurement and deficit calculation	Within Theatres CAH a dedicated Fluid Balance Nurse has been appointed ATICS have developed their own fluid management documentation sheets and these are currently in use.		The regionally agreed perioperative fluid recording chart is to be implemented within all relevant theatre areas. To be appendiced within the new Standard Operating Procedures for the Management of irrigation fluids for patients undergoing TCRE / TCRF / TURP /TURB/TART	Mary McGeough Head of ATICS Brigeen Kelly Lead Nurse ATICS	31/12/2015

6. For both mono- and bi-polar techniques, limit the distension pressure by, a. maintaining it below the mean arterial pressure (MAP).	A draft Standard Operating Procedure for the Management of irrigation fluids for patients undergoing TCRE / TCRF / TURP /TURB/TART procedures is currently being developed		These draft standard operating procedures need to be reviewed in line with the requirements of the new regional policy, agreed and then implemented within the Trust.	Mary McGeough Head of ATICS Brigeen Kelly Lead Nurse ATICS	31/12/2015
With continuous-flow gravity systems, b. limit the height of the irrigating solution container to 60 cm above the patient and certainly never above 100cm; c. theatre teams must have a procedure for checking and maintaining an agreed height; d. not applying pressure bags to the irrigation fluid bag.	A draft Standard Operating Procedure for the Management of irrigation fluids for patients undergoing TCRE / TCRF / TURP /TURB/TART procedures is currently being developed		The draft standard operating procedures need to be reviewed in line with the requirements of the new regional policy, agreed and then implemented within the Trust.	Mary McGeough Head of ATICS Brigeen Kelly Lead Nurse ATICS	31/12/2015
7. Investigate instilling irrigation fluid by using a pressure controlled pump device and purchasing flow/pressure controllers.	Infusion pumps are used by gynae teams Infusion pumps are not used by urology teams because at present the pumps are not deemed suitable		No action required Work is currently being carried out by Lead Urology Consultant and equipment supplier to improve the efficiency of the pumps for urology purposes – at present the pumps are not suitable. In the meantime flow is being regulated as per 6(a) and 6 (b)	- Urology Consultants led by Mr Young	- 31/12/2015

			If the equipment is deemed suitable sufficient funding will be required to ensure procurement can proceed	Dr Wright Medical Director	31/03/2016
8. The theatre team **must,** a. be aware of the distending fluid input & output and deficit; b. contain a dedicated nurse for fluid balance and deficit calculation, who remains in theatre for the duration of the procedure	Within Theatres CAH a dedicated Fluid Balance Nurse has been appointed ATICS have developed their own fluid management documentation sheets and these are currently in use.		The regionally agreed perioperative fluid recording chart is to be implemented within all relevant theatre areas. To be appendiced within the new Standard Operating Procedures for the Management of irrigation fluids for patients undergoing TCRE / TCRF / TURP /TURB/TART	Mary McGeough Head of ATICS Brigeen Kelly Lead Nurse ATICS	31/12/2015
9. If continue to use glycine, the following **must** be used, throughout the procedure, a. accurate irrigation fluid input & output measurement and deficit calculation	This monitoring process is in place irrespective of whether glycine or saline is being used		On-going monitoring and review of both glycine and saline	All staff involved in this clinical task	On-going
10. Preoperatively, for each individual patient, there **must** be an agreed maximum fluid deficit threshold for action. The surgeon and anaesthetist **must** be informed by the nurse when the threshold is reached.	Within the SHSCT there is no specified individualised threshold. Within the Gynae and Urology teams, the surgeon and anaesthetist must be notified when the maximum fluid deficit threshold		The draft standard operating procedures need to be reviewed to ensure the agreed maximum fluid deficit threshold for notification and stopping surgery is	Mary McGeough Head of ATICS Brigeen Kelly Lead Nurse ATICS	31/12/2015

	is over 500 and then go no further when the maximum fluid deficit threshold is at 1000		specified.		
11. Operations should, if possible, not last longer than 60 minutes, a. Theatre teams **must** have an established mechanism for measuring time and procedures for alerting surgeon and anaesthetist.	The recording of resection time is adhered to. It is also a required field within the ATICS fluid management documentation sheet		The draft standard operating procedures need to be reviewed to ensure this requirement is specified prior to implementation within the Trust.	Mary McGeough Head of ATICS Brigeen Kelly Lead Nurse ATICS	31/12/2015
12. Completion of the standard WHO surgical checklist **must** be adhered to. Adoption of a modified WHO checklist for this kind of procedure should be investigated and piloted	Completion of the standard WHO surgical checklist is adhered to.		The Trust has taken the stance that the WHO checklist will not be modified for this kind of procedure since deviance from the standardised WHO checklist could create its own set of risks for the organisation	Ongoing	Ongoing

Identified Limiting Factors for preventing full compliance against guidance recommendations:
1. Required funding for the purchase of 5 new ISTAT point of care machines – cost is estimated at £27k 2. Complete trial of bipolar resection equipment within Urology services to ascertain if it is feasible to remove the need to use glycine – amount of funding required if trial outcomes are favourable is to be determined 3. Ascertain if infusion pumps can be used within urology Services. If deemed suitable for use within Urology Services, funding needs to be prioritised and allocated for the procurement of these devices. Amount of funding required if trial outcomes are favourable is to be determined 4. Finalisation of the Standard Operating Procedure for the Management of Irrigation Fluids for patients undergoing TCRE / TCRF / TURP /TURB/TART procedures 5. Need to replace the existing fluid management documentation with the new regional perioperative fluid recording chart and advise staff of any changes to recording requirements. This new recording chart is to be included within the new standard operating procedure referenced in point (4)

Compliance Scale:

100% Compliance	70-99% Compliance	40-69% Compliance	0-39% Compliance	Pending	Not Applicable

Corrigan, Martina

From: Haynes, Mark [redacted]
Sent: 31 December 2014 14:12
To: O'Brien, Aidan
Cc: Corrigan, Martina; Glackin, Anthony; Haynes, Mark; Suresh, Ram; Young, Michael
Subject: RE: Medical Leaders Forum 3rd November 2014

And
'The presentation outlined comparisons between techniques supported by evidence, from various sources such as NICE, Royal College of Obstetricians and Gynaecologists, The Cochrane Collaboration, BUPA and the British Fibroid Trust, …'

Presumably BAUS and the RCS have limited experience of glycine use and it was considered that evidence from urological surgeons was of limited use? I fear however that the tide has turned and fear is driving this, to fight against it will be swimming against the current.

Our response should highlight the not insignificant cost of switching to bipolar as all of our resection equipment would need replacing and would be a significant outlay for the trust. We also need to be clear that the fluid management system which has been purchased by the trust is not fit for purpose from a urological perspective and will not be used unless modifications are made which render it fit for purpose.

Mark

From: O'Brien, Aidan
Sent: 30 December 2014 20:46
To: Corrigan, Martina; Glackin, Anthony; Haynes, Mark; Suresh, Ram; Young, Michael
Subject: RE: Medical Leaders Forum 3rd November 2014

Dear All,

I believe that it is important that all of you are aware of the contents of the section 'Endoscopic Distending Fluids – Urology and Gynaecology'.
Whilst there is some circumspection regarding the phasing out of the use of Glycine, and the instigation of safety measures if it's use is continued, I still do have the following concerns:

· The report has been compiled by an anaesthetist who can never performed a prostatic or bladder tumour resection
· The conflation of the use of glycine in gynaecological and urological practice
· In arriving at a 'collegiate' and 'regional' policy, Dr. Johnston is to have further discussions with consultants, relevant clinical teams and personnel in BHSCT!

Could we have a further discussion of this matter or should we allow sleeping dogs lie?

Aidan

From: Corrigan, Martina
Sent: 29 December 2014 17:56
To: Glackin, Anthony; Haynes, Mark; O'Brien, Aidan; Suresh, Ram; Young, Michael
Subject: FW: Medical Leaders Forum 3rd November 2014

Dear all

FYI

Martina

Martina Corrigan
Head of ENT, Urology and Outpatients
Southern Health and Social Care Trust
Craigavon Area Hospital

Telephone: Personal Information redacted by the USI
Mobile: Personal Information redacted by the USI
Email: Personal Information redacted by the USI

From: Burns, Deborah
Sent: 17 December 2014 14:57
To: Mackle, Eamon; Young, Michael; Sim, David; McCracken, Geoff; McVey, Anne
Cc: Trouton, Heather; Corrigan, Martina
Subject: FW: Medical Leaders Forum 3rd November 2014

See below

Debbie Burns
Acting Director of Acute Services
SHSCT
Personal Information redacted by the USI
Tel: Personal Information redacted by the USI

From: Simpson, John
Sent: 17 December 2014 11:10
To: Hogan, Martina; McCracken, Geoff; McVey, Anne; Marshall, Margaret
Cc: Burns, Deborah
Subject: FW: Medical Leaders Forum 3rd November 2014

Dear All,
See item 2 fyi
john

From: Rocks, Dennis Personal Information redacted by the USI
Sent: 17 December 2014 09:08
To: Dr Alan McKinney; Dr Alan McKinney - PA; Dr Alan McKinney - PA; Dr Cathy Jack; Dr Cathy Jack - PA; Dr Greg Furness; Dr Greg Furness - PA; Simpson, John; Feely, Roisin; Mr Charlie Martyn; Mr Charlie Martyn - PA; NI Ambulance Service; NI Ambulance Service - PA; Carolyn Harper; David Stewart; Dawn Clarke's email address Dowie Joanne; Dr Gavin Lavery; Morris Kieran; PA - Dr Carolyn Harper; PS - Dr David Stewart; Sloan Harper; Tom Trinick; Keith Gardiner; Prof. Pascal McKeown; Prof. Pascal McKeown - PA; Prof. Stuart Elborn; Pauline Dardis; PS Prof Elborn; McArdle, Charlotte; Henderson, Elizabeth
Cc: Bradley, Fergal
Subject: Medical Leaders Forum 3rd November 2014

Apologies

Draft minutes attached
++
All

Please see attached draft minutes of meeting on 3rd November 2014

Would you please review relevant content under organisational updates and reply with any suggested changes

Thank You

Dennis

Stinson, Emma M

From: Young, Michael [redacted]
Sent: 04 March 2015 18:41
To: O'Brien, Aidan; ODonoghue, JohnP; Glackin, Anthony; Suresh, Ram; Haynes, Mark
Cc: Corrigan, Martina; [redacted]
Subject: FW: Endoscopic Distending fluids
Attachments: Policy on surgery for endoscopic tissue resection V0.3.docx

Important info

From: Johnston, Julian [redacted]]
Sent: 27 February 2015 16:58
To: Young, Michael; 'McKnight, John'; McAllister, Charlie; Hagan, Chris; 'Darling, John'; [redacted] McCracken, Geoff; [redacted] McClelland, Raymond; [redacted]
Cc: Simpson, John; 'Alan McKinney [redacted] Jack, Cathy; [redacted]
Subject: Endoscopic Distending fluids

Please attached a second draft policy setting out a proposed 'collegiate' view for managing endoscopic tissue resection.
I have taken into account views expressed to me following the first time I sent out a draft policy.
I have also examined in detail the recent literature and documents from NICE and the Cochrane Collaboration.
This document has been substantially modified and forms the basis of presentations to the Medical Leaders Forum.

It details a direct of travel. My inquiries and those of leaders in urology and gynaecology indicate that there is now support for what is described.
If a sizeable majority of urologists and gynaecologists are in agreement, then that will be the direction proposed to the Trusts MDs and the CMO.

I would like views expressed to me by 15th March 2015 please.
Please circulate this to interested colleagues who are not on the email list above. I think I am missing the names of some Urologists.

Regards,

Julian R Johnston MD FCARCSI FRCA
Assistant Medical Director
BHSCT
[redacted]

Co-Chair Standards and Guidelines Committee Standards, Quality and Audit department
Telephone: [redacted]

If unanswered, contact Christine Murphy : Personal Information redacted by the USI or Jill Shaw O'Doherty : Personal Information redacted by the USI or Simon Dunlop : Personal Information redacted by the USI

BHSCT Litigation Management Office
Telephone: Personal Information redacted by the USI
If unanswered, contact Ann Maginnis: Personal Information redacted by the USI or Amanda Lennon (Coroner's Office): Personal Information redacted by the USI or Susan McCombe (Clinical Negligence): Personal Information redacted by the USI or Lorraine Watson (BCH Clin. Neg./Coroner's) Personal Information redacted by the USI.

Trust LOGO

Reference No:

Title:	Policy on the surgical management of endoscopic tissue resection, for example during urological, gynaecological and other relevant surgery.		
Author(s)	List name and titles of lead and additional author(s) or group responsible for drafting policy Include contact details		
Ownership:	Insert name of Director / service area / group / directorate		
Approval by:	Insert name of Trust committee / group responsible for approval	**Approval date:**	Insert date each committee approved
Operational Date:	March 2015	**Next Review:**	March 2017
Version No.	V0.3	**Supercedes**	Any legacy policies.
Key words:	Endoscopic, Resection, Prostatectomy, Myomectomy, TUR syndrome		
Links to other policies			

Date	Version	Author	Comments
20/11/2013	0.1	SE Trust	Initial Draft
03/12/2013	0.2	JR Johnston	Amalgamation of protocols from 5 Trusts.
01/02/2015	0.3	JRJ	Following 3/11/14, 19/01/2015 MLF meetings

Recommendations

All of the surgical (urology, gynaecology) teams in NI practicing this type of surgery should become fully cogniscent of the risks of the TUR syndrome and work together to develop a co-ordinated 'collegiate' regional approach where they take steps to,

- agree a programme of change for the cessation of glycine use.
- develop or adopt techniques that do not rely on glycine as an irrigant.
- use equipment designed to control or reduce vesical or uterine pressure.
- establish a set of safe practice standards.

1. Preoperative workup needs geared towards prevention of the TUR syndrome.
2. Introduce Bipolar equipment using saline; curtail the use of glycine as a irrigant, strictly monitor when it is still used and eventually stop when there ceases to be circumstances when glycine use is considered the safest.
3. Engineer changes in the type of procedures performed.
    a. More 2° procedures for management of heavy menstrual bleeding as per NICE recommendations.
4. Increase vigilance when significant haemorrhage is a feature.
5. If continue to use glycine, the following MUST be used,
    a. Measure POCT serum sodium.
        i. preoperatively.
        ii. if the surgery is longer than 30 mins.
        iii. intermittently throughout the surgery.
        iv. if there is a 1000 mls fluid deficit.
    b. Dedicated staff for transporting specimens and results.
    c. Surgery, including TCRE & TCRF, must be performed in a 'main' theatre where POCT equipment is immediately available.
6. Limiting the distension pressure by,
    a. maintaining it below the mean arterial pressure (MAP).
    b. attempting to limit the height of the irrigating solution container to 60 cm above the patient and certainly never above 100cm.
    c. Theatre teams must have a procedure for checking and maintaining an agreed height.
    d. not applying pressure bags to the irrigation fluid bag.
7. Investigate instilling irrigation fluid by using a pressure controlled pump device and purchasing flow/pressure controllers.
8. The theatre team must,
    a. be aware of the distending fluid input & output and deficit.
    b. contain a dedicated nurse for fluid balance and deficit calculation, who remains in theatre for the duration of the procedure.
9. If continue to use glycine, the following MUST be used, throughout the procedure,
    a. Accurate fluid measurement and deficit calculation.
10. Preoperatively, there must be an agreed maximum fluid deficit threshold for action. The surgeon and anaesthetist must be informed by the nurse when the threshold is reached.
11. Operations should not last longer than 60 minutes
    a. Theatre teams must have an established mechanism for measuring time and procedures for alerting surgeon and anaesthetist.
12. Completion of the WHO surgical checklist must be adhered to. Adoption of a modified WHO checklist for this kind of procedure should be investigated and piloted.

1.0 INTRODUCTION / PURPOSE OF POLICY

1.1 Background

Some endoscopic surgical procedures require the use of an irrigating fluid to distend the operating field to enable a suitable field of vision and to wash away debris and blood. This includes operations such as,

- resection of prostate (TURP) and bladder tumours (TURBT).
- transcervical resection of endometrium (TCRE), transcervical resection of fibroids (TCRF).
- removal of uterine septum, polyps, endometrial ablations.
- cystoscopy, arthroscopy, rectal tumour surgery, vesical ultrasonic lithotripsy and percutaneous nephrolithotripsy.

A serious complication of such irrigation is the systemic intravascular absorption of the irrigation fluid to the extent that serious overt symptoms are produced[1].

This policy sets out the steps needed to reduce the risks of that happening. Using the national policies, guidelines and evidence identified in section 7 along with on-going work within the province, its aim is to establish a regionally agreed,

- plan to use the safest resection technique with its attendant fluid,
- set of precautions to minimise the risk of intravascular absorption.

Some of the recommendations can be instituted now and some will depend on the financing of equipment.

1.2 Irrigation fluids used

The irrigation fluid used for these electrosurgical procedures should,

- have neutral visual density so that the surgeon‘s view is not distorted.
- be nonconductive so the electrical current is not dissipated and can remain concentrated at the cutting point.
- be non-haemolytic and will not lead to haemolysis if it enters the circulation.

In the past, **sterile water** was used as the irrigant but was associated with significant morbidity because of water intoxication and intravascular haemolysis.

Modern non-electrolytic solutions containing glycine 1.5%, mannitol or sorbitol are optically clear and were introduced to prevent haemolysis, without dispersing the electric current used for cutting with the resectoscope. Their use in irrigation solutions has reduced the occurrence of significant haemolysis and death.

The most commonly used irrigation fluid has been 1.5 % **glycine solution,** a non-essential amino acid with a low cost and lack of allergic reactions**.** However, it has an osmolality of 200 mOsm/L which is much lower than that of blood [Plasma = 290 mosmol.kg^{-1}] and large amounts of this hypotonic irrigation fluid, required to facilitate the procedure, may be absorbed

systemically through a vascular bed[2]. This may cause several serious complications known as the **TUR syndrome** which can occur in a variety of surgical disciplines.

Normal saline is used for irrigation with the bipolar resectoscope. It is associated with fewer unfavorable changes in serum sodium and osmolality than is the case when electrolyte-free media are used with monopolar systems[3] e.g. glycine. Its use, however, does not eliminate the need to prevent excess absorption or to closely monitor fluid balance, as overload can occur. Pulmonary oedema is a reported consequence. Moreover, it can cause hyperchloraemic acidosis due to its excessive content of chloride.

1.3 TUR syndrome[4]

This is an iatrogenic form of acute water intoxication from a combination of fluid overload and hyponatraemia. It is manifested mainly through a classic triad of,

- fluid overload - acute changes in intravascular volume leading to circulatory overload, pulmonary oedema, cardiac failure and even cardiac arrest.
- dilutional hyponatraemia causing central nervous system (CNS) effects such as cerebral edema leading to agitation, confusion, convulsions and coma.
- direct toxicity and metabolism of glycine which may also cause CNS symptoms, most commonly transient blindness and CNS depression as it is an inhibitory neurotransmitter. Its metabolism yields water (worsening fluid overload) and ammonia.

1.4 Purpose

This policy outlines a set of principles designed to reduce the development of the TUR syndrome.

1.5 Objectives

To reduce the likelihood of developing the TUR syndrome through,

- correct patient selection and preoperative preparation.
- selection of an appropriate surgical technique.
- electing to use surgical equipment which allows the use of irrigation fluid which will not give rise to the TUR syndrome.
- the application of monitoring aimed at detecting the early warning signs of the TUR syndrome.
- establishing a theatre regime based on good theatre practice principles aimed at reducing the development of the TUR syndrome.

2.0 SCOPE OF THE POLICY

This policy applies to all staff who may be involved in the care of a patient in theatre who receives irrigating fluid into the bladder or uterus or any other organ where significant fluid absorption is a realistic possibility.

It applies to medical staff, nursing staff, midwives, operating department practitioners, technical staff, physicians' assistants (anaesthesia) and other theatre healthcare workers.

This policy does not cover the methods of treatment of the TUR syndrome.

3.0 ROLES/RESPONSIBILITIES

Medical staff - careful consideration of the therapeutic choices, when planning the service for endoscopic resection, can reduce the likelihood of the development of the TUR syndrome.

Management – actively supporting the introduction of therapeutic modalities that aim to reduce the incidence of the TUR syndrome.

All staff involved in the care of the patient, especially in theatre, are responsible for implementing and adhering to the policy principles.

Each ward/theatre sister/charge nurse/clinician involved with this kind of surgery is responsible for ensuring staff comply with this policy and all relevant staff have the responsibility to ensure that they read and comply with the policy contents.

In the event of an untoward incident an adverse incident form must be completed by either the medical officer or nurse in charge of the patient's care.

4.0 POLICY PRINCIPLES

4.1 Definitions

Osmolality: The concentration of osmotically active particles in a solution.

Hypertonic: Higher osmolality (concentration of particles) than that found in normal cells.

Hypotonic (or hypo-osmolar): Lower osmolality (concentration of particles) than that is found in normal cells.

Hyponatraemia: Lower sodium concentration than normally found in plasma.

Resectoscope: An endoluminal surgical device comprising an endoscope (hysteroscope or cystoscope), sheaths for inflow and outflow, and an ''element'' that interfaces a specially designed electrode (or pair of electrodes) with a radiofrequency (RF) electrosurgical generator which can be either monopolar or bipolar.

4.2 Policy Principles

An irrigating fluid is most frequently absorbed directly into the vascular system when a vein has been severed by electrosurgery. The driving force is the fluid pressure; the volume of fluid absorbed depending on the,

- duration of the procedure and resection time,
- degree of opening of blood vessels during surgery ,
    - vascularity of the diseased prostate, uterus, fibroid.
    - surgical disruption of the bladder, uterine vessels.

- capsular or uterine wall perforation or apparent damage to a venous sinus.
- pressure of the distending fluid within the bladder or uterus,
  - height of the irrigation fluid bag above the patient.
  - distension pressure applied to the irrigation fluid.

For safe endoscopic resection using irrigation fluid, consideration of the following topics needs covered,

a. Preoperative workup.
b. Selection of surgical technique.
c. Identification, control and management of haemorrhage.
d. Control of the absorption of irrigation fluid.
   a. Dilutional Hyponatraemia.
   b. Fluid overload.
   c. Glycine toxicity.
e. Theatre environment.
   a. Decision making processes.
   b. Team dynamics.
   c. Knowledge of potential complications.

4.2.1 Preoperative workup

Careful preoperative workup of the patient must include, for example,

- a robust consent process leading to a truly informed patient aware of the hazards of endoscopic resection using irrigation fluids.
- a thorough physiological assessment with attention paid to risk factors such as hypertension, ischaemic heart disease, cardiac failure, anaemia.
- standard haematology and electrolyte analysis - to include a recent haemoglobin, serum sodium.
- careful consideration regarding blood grouping and cross-matching.
- recent investigations aimed at establishing the pathological anatomy and degree of surgical risk especially haemorrhage e.g. ultrasound scan.
- the ready availability of reports of such investigations before surgery commences.

Recommendation 1
Preoperative workup needs geared towards prevention of the TUR syndrome.

Urology

These procedures are carried out on a predominantly elderly population with a high incidence of coexisting disease. BPH affects 50% of males at 60 years and 90% of 85-year-olds and so TURP is most commonly performed on elderly patients, a population group with a high incidence of cardiac, respiratory and renal disease.

Gynaecology

Consideration should be given to the timely commencement of any adjuvant therapy prior to the surgery[3], especially if it helps to reduce the risk of haemorrhage and/or causes a reduction in tumour size.

4.2.2 Selection of surgical technique

Urology
Absorption in excess of 1 litre of glycine solution, which is associated with a statistically increased risk of symptoms, has been reported in 5–20% of the TURPs performed[1].

The development of bipolar radiofrequency (RF) instrumentation for endoscopic resection procedures addresses the fundamental flaw of monopolar equipment by allowing performance in a normal saline irrigation. Therefore, the adoption of bipolar TURP/TURBT allows NS irrigation in urology and permits the removal of glycine and its inherent risks from theatre. The risks of the hyponatraemic and hypo-osmolar aspects of the TUR syndrome are eliminated.

The TUR syndrome has not been reported with bipolar equipment[5]. There is now increasing recent evidence[6 - 9] for the effectiveness and safety of bipolar systems as their technical performance has been developed and improved. TUR syndrome was reported in 35/1375 patients undergoing monopolar TURP and in none of the 1401 patients undergoing bipolar TURP[9]. Recent systematic reviews[7, 9] are repeatedly describing equal effectiveness between monopolar and bipolar techniques but with a significantly improved safety profile for bipolar. Indeed there is some evidence[9] that bipolar may be better at improving urine flow rates and also reducing bleeding related complications as well as eradicating the TUR syndrome. With reduced bleeding and improved visibility, resection time can be decreased.

NICE now recommends[10] that bipolar techniques are associated with lower rates of complications and they now support[11] the use of transurethral resection in saline which eliminates the TUR syndrome and may also reduce length of stay as well as having cost benefits.

However, it should be remembered that the use of NS is not without risk because there will still be fluid absorption with plasma volume expansion.

As long as they are proven to be safe and effective as judged by the NICE interventional procedure programme, bipolar RF systems and other technique e.g. laser systems, should be introduced regionally and the use of glycine as a irrigant curtailed, strictly monitored when it is still used and eventually terminated when there ceases to be circumstances when its use is considered the safest.

Recommendation 2
Introduce Bipolar equipment using saline regionally; curtail the use of glycine as a irrigant, strictly monitor when it is still used and eventually stop when there ceases to be circumstances when glycine use is considered the safest.

Gynaecology

The first generation endometrial ablative techniques including transcervical resection of endometrium (TCRE) and rollerball endometrial ablation (REA) are all endoscopic procedures. Fluid absorption is slightly more common during TCRE than during TURP, with transcervical resection of fibroids (TCRF) being at a further increased risk over TCRE. As TCRE often evolves into a TCRF when fibroids are found during hysteroscopy, it means the same safety procedures need to be put into place for both TCRE and TCRF.

Their effectiveness in the management of heavy menstrual bleeding (in comparison with hysterectomy - the existing gold standard) has been demonstrated in a number of randomised controlled trials. Although less morbid than hysterectomy, they are associated with a number of complications including uterine perforation, cervical laceration, false passage creation, haemorrhage, sepsis and bowel injury and, importantly, the fluid overload and hyponatraemia associated with the use of 1.5% glycine irrigation fluid resulting in the serious and occasionally fatal consequences discussed above.

However, there are now second generation ablative techniques which do not require the use of electrocautery or the use of glycine or other distension fluids. They avoid the serious risk of hyponatraemia and represent simpler, quicker and potentially more efficient means of treating menorrhagia.

A Cochrane Collaboration review (2013)[12] concludes that “Overall, the existing evidence suggests that success, satisfaction rates and complication profiles of newer techniques of ablation compare favourably with hysteroscopic techniques.”

NICE[13] in their online guidance for Heavy Menstrual Bleeding recommend,

- First-generation ablation techniques (e.g. rollerball endometrial ablation [REA] and TCRE) are appropriate if hysteroscopic myomectomy (TCRF) is to be included in the procedure.

- All women considering endometrial ablation should have access to a second-generation ablation technique.

Recommendation 3
Engineer changes in the type of procedures performed. • More 2° procedures for management of heavy menstrual bleeding as per NICE recommendations.

If hysteroscopic procedures such as TCRE and TCRF are considered to be the best options and a distending fluid is required, the choice of fluid then comes under the same scrutiny as above for Urology. The choice of using a monopolar scope system using glycine versus bipolar equipment using saline becomes the choice. Evidence is now emerging from gynaecology units in Northern Ireland that are measuring the serum sodium intraoperatively during every case, that there can be concerning incidences of acute hyponatraemia

when glycine is used as the distending agent during TCRE[14]. With the development of newer bipolar systems it is recommended that saline has a better safety profile[3].

Therefore, this policy recommends that, (as long as they are proven to be safe and effective as judged by the NICE interventional procedure programme,) the use of second generation ablative techniques and bipolar RF systems should be introduced regionally and the use of glycine as a irrigant curtailed, strictly monitored when it is still used and eventually terminated when there ceases to be circumstances when its use is considered the safest.

4.2.3 Identification, control and management of haemorrhage.

Blood loss can be difficult to quantify and may be significant. Close attention to the patient's clinical state and good communication between surgeon, anaesthetist and the theatre team is vital.

Because of the generalised physiological effects of haemorrhage and the increased likelihood of fluid absorption when using irrigation fluid in the presence of 'open' vasculature, the presence of significant bleeding should act as a trigger for,

- increased vigilance for development of fluid overload, hyponatraemia.
- additional help from medical and nursing staff to assist by scrubbing in.
- increased frequency of haemoglobin and/or haematocrit measurements.
- preparation of blood for cross matching.
- control of the bleeding which may need cessation of the operation.

Recommendation 4
Increase vigilance when significant haemorrhage is a feature.

4.2.4 Control of the absorption of irrigation fluid

To control the effects of fluid absorption, the theatre team should pay particular attention to,

a) hyponatraemia.
b) limiting the volume of fluid absorbed.

a. Hyponatraemia

The uptake of 1000 ml of fluid would generally correspond to an acute decrease in the serum sodium concentration of 5-8 mmol/L.[2] Encephalopathy, seizures and even cerebral oedema may develop when the sodium concentration falls below 120mmol/l. However, even markedly hyponatraemia patients may show no signs of water intoxication. The crucial physiological derangement of CNS function is not just hyponatraemia *per se*, but also the presence of acute hypo-osmolality[4].

Also, a patient's serum sodium concentration and osmolality may continue to decrease for some time after the procedure because irrigant can be slowly absorbed from the perivesicular and retroperitoneal spaces. Therefore, the

TUR syndrome can start 4 to 24 hours later – postoperatively, in the recovery ward or back in the ward.

Whereas hyponatraemia occurs with equal frequency in men and women, premenopausal women are 25 times more likely to die or have permanent brain damage than men or postmenopausal women, most likely an oestrogen effect[3]. This effect is compounded because fluid absorption is slightly more common during TCRE than during TURP, and especially so with TCFR.

Serum Sodium measurement
Monitoring serum sodium concentration during TURP is common practice and a low value will confirm the diagnosis of hyponatraemia and is effective for assessing intravascular absorption. Significant decreases from a normal preoperative level can occur after just 15 minutes of starting resection. Levels below 120 mmol/L are invariably symptomatic and a rapid fall is more likely to produce symptoms.

Point-of-care testing (POCT) is defined as medical testing at or near the site of patient care. It brings the test conveniently and immediately to the patient increasing the likelihood that the patient, physician, and care team will receive the results in minutes, enabling diagnosis of hyponatraemia as early as possible and allowing immediate clinical management decisions to be made. They can be used to measure haematocrit, determine haemoglobin and measure serum electrolytes.

Serum sodium is often only measured at the end of surgery but, in the surgical settings pertaining herein, this monitoring technique is best applied before and repeatedly during surgery so that it can act as a warning system for hyponatraemia. Trusts already operating this method of monitoring have uncovered episodes of unsuspected hyponatraemia; highlighting the need to be wary of glycine and to monitor accordingly. Previous audits that have not measured serum sodium as part of their audit criteria are thus likely to have given a false sense of security when using glycine.

Any patient receiving glycine in theatre **must** have such POCT equipment available and a measurement(s) made,

- as a preoperative baseline prior to the start of surgery.
- if the surgery is longer than 30 minutes.
- intermittently throughout a case as a routine.
- if there is a 1000ml fluid deficit.

Staff must be readily available who are trained to use this POCT equipment and indeed immediately available to transport the samples and result to and from the machine.

NOTE: Measurement of serum sodium is not required when using a bipolar technique and saline[8].

Recommendation 5
If continue to use glycine, the following MUST be used, • Measure POCT serum sodium. i. preoperatively. ii. if the surgery is longer than 30 mins. iii. intermittently throughout the surgery. iv. if there is a 1000 mls fluid deficit. • Dedicated staff for transporting specimens and results. • Surgery, including TCRE & TCRF, must be performed in a 'main' theatre where POCT equipment is immediately available.

b. <u>Limit the volume of fluid absorbed.</u>
The choice of surgical technique and equipment may reduce the complications from irrigation fluid by limiting the use of glycine but continued attention to controlling fluid absorption will still be needed if normal saline is used as the distending fluid.

Basic principles govern the amount of fluid absorbed[15].

i. The hydrostatic driving pressure of the distending fluid. This is often a feature of the height of the container but the pressure may be controlled mechanically.
ii. Measurement, monitoring and documentation of the fluid volumes and deficits.
iii. The length of the surgical procedure.

i. Hydrostatic driving pressure of the distending fluid
Surgeons have a vital role in minimising absorption by keeping the cavity distention pressure at the lowest pressure necessary to distend, consistent with good visualisation and ideally should be maintained below the mean arterial pressure (MAP).

It is estimated that approximately 40mmHg distending pressure is required to obtain clear vision. At pressures between 40mmHg and approximately 100mmHg (MAP), blood will continue to escape from disrupted capillaries until it is stopped by the tamponade. At this point, when continuous flow is used through the resectoscope, the blood within the cavity will be removed and a clear field of vision will be maintained. Dropping the pressure permits further bleeding. If the pressure is raised above the MAP, the pressure not only prevents the flow of blood out of disrupted vessels but actually forces the distension fluid medium in the reverse direction into the vessels.

There exist a number of fluid delivery systems, ranging from those based on simple gravity to automated pumps that are designed to maintain a pre-set intra-cavity pressure. Methods of instilling the distention fluid include,

- continuous-flow gravity,
- continuous-flow infusion pump,
- pressure-controlled or pressure-sensitive fluid pumps.

Continuous-flow gravity

In continuous-flow gravity systems, pressure is controlled by the height of the fluid source above the bladder or uterus and is measured from the height of the highest portion of the continuous column of fluid (fluid bag) to the level of the uterus or bladder – approximately 30 cms height is equivalent to 25 mm Hg pressure[16]. If the bag is 60 cms above the patient's uterus, this results in approximately 50 mm Hg of pressure.

Height of fluid column	Pressure exerted
12 inches ≡ 30 cms	25 mmHg
24 inches ≡ 60 cms	50 mmHg
36 inches ≡ 90 cms	75 mmHg

Gravity based systems are very simple to assemble and operate, but require vigilant patient monitoring and frequent manual intake/output calculations, which can be imprecise.

Recommendation 6
Limiting the distension pressure by, • maintaining it below the mean arterial pressure (MAP). • attempting to limit the height of the irrigating solution container to 60 cm above the patient and certainly never above 100cm. • Theatre teams must have a procedure for checking and maintaining an agreed height. • not applying pressure bags to the irrigation fluid bag.

Continuous-flow infusion pump

Continuous-flow fluid infusion pumps provide a constant flow of distention fluid at the in-flow pressure determined by the operator, delivering the same flow rate regardless of the out-flow conditions. Continuous flow pumps do not usually monitor or calculate the intracavity pressure. Significant fluid absorption and complications can occur with these types of systems because the team is unaware of the actual pressure being used during a prolonged or invasive procedure.

Pressure-controlled or pressure-sensitive fluid pumps

Pressure-controlled infusion pumps can be preset to maintain a desired in-flow pressure. By adjusting the in-flow pressure setting on the pump, it can be maintained below the MAP, thus reducing the likelihood of intravasation.

These pumps can weigh the fluid volume before infusion, which allows them to account for the overfill often found in fluid bags. Weight of fluid before installation and then after, accounts for the deficit, which provides a more accurate measurement of the fluid retained by the patient (fluid deficit). A continuous automated weighing system provides an easy, less time-consuming and valid method of monitoring fluid deficit[2] and an automated fluid management system is recommended[3].

Recommendation 7
Investigate instilling irrigation fluid by using a pressure controlled pump device and purchasing flow/pressure controllers.

ii. Measurement, monitoring and documentation of the fluid volumes & deficits.
If continuous irrigation using fluid filled bags and gravity continue to be used, volumetric fluid balance is based on counting the number of empty fluid bags and then subtracting the out-flow volume in the collection canister and fluid in the drapes to determine fluid deficit. Positive values are regarded as absorption. The surgeon should be notified about ongoing fluid absorption early enough for steps to be taken to prevent excessive absorption.

However[1], calculation of systemic absorption is complicated by 4 factors:
1. It may be difficult to collect all of the media (fluid, urine and blood) that passes out of the operative area, including that which falls on the procedure or operating room floor.
2. the actual volume of media solution in 3L bags is typically more than the labelled volume.
3. difficulties in estimating the volume of media left in a used or 'emptied' infusion bag.
4. systemic absorption that in some instances may occur extremely rapidly.

While these factors can make volumetric fluid balance measurement an unreliable tool, it is considered a minimum necessity when using fluid filled bag systems that the whole theatre team are aware of the distending fluid input & output and the deficit. This is especially true for cases where glycine is used.

A member of staff must be assigned to this duty before the start of every case. They will need to be proficient and practiced in this technique and must take responsibility for measuring the input and output, calculating the deficit and recording these details. They should remain in theatre for the duration of the procedure, in the same fashion as the surgeon.

Recommendation 8
The theatre team must, • be aware of the distending fluid input & output and deficit. • contain a dedicated nurse for fluid balance and deficit calculation, who remains in theatre for the duration of the procedure.

When using a pressure-controlled infusion pump to control the distension fluid with their associated continuous automated weighing system, the monitoring of the fluid deficit is easier[2], less time-consuming and thus an automated fluid management system is recommended[3].

Documentation
Each patient who has any irrigating fluid used must have documentation in the way of a dedicated fluid management chart (appendix 1) commenced. This can be either the measurement of input & outputs and calculating the deficit or recording the readings off an automated machine.

This should be done as a minimum every time a bag (often 3 litre) is hung up and the details clearly expressed verbally to the surgeon and all other theatre staff. These details should be recorded on the dedicated fluid management chart. They might also be displayed on a white marker board in the theatre.

At the end of the procedure, the final calculations or readings must be made; the inputs, outputs and deficit. These should be expressed clearly to the surgeon and anaesthetist and recorded on the chart. The operating surgeon should include the fluid deficit in the *Operative Findings* when writing the operative notes

The fluid management chart must follow the patient into the recovery ward. All fluid balances must be handed over to recovery ward staff as part of the normal nursing and medical handover. The chart is then to be filed in the clinical record.

Recommendation 9
If continue to use glycine, the following MUST be used, throughout the procedure, • Accurate fluid measurement and deficit calculation.

Maximum fluid deficit
Prevention of the TUR syndrome requires that the team have a protocol for responding to any escalating fluid absorption and there must be agreed volume thresholds for action. These thresholds may necessarily vary depending on the,

- nature of the surgery,
- nature of the media (isotonic or hypotonic) ,
- patient's baseline,
- intraoperative medical condition e.g. presence of haemorrhage.

Considering glycine use, a 500 ml threshold may be appropriate for those who are older and/or medically compromised while for healthy individuals absorption of up to 1000 mL can generally be tolerated. Greater than 1000 mL of glycine intravasation results in a significant decrease in serum sodium, sufficient to bring a normo-natraemic patient into the abnormal range[1, 2, 3].

The surgeon and anaesthetist must be informed by the nurse when there is a 1000mls deficit. Surgery must be brought to a close unless continuation of surgery is absolutely necessary to control the haemorrhage. The nurse must ensure that the surgeon and anaesthetist acknowledge that they have

received this information. This must be documented in the notes along with any action taken.

Considering normal saline use, the maximum limit is unclear, but 2500 mL has been advocated[3]. Surgery must be brought to a close unless haemorrhage needs controlled.

Recommendation 10
Preoperatively, there must be an agreed maximum fluid deficit threshold for action. The surgeon and anaesthetist must be informed by the nurse when the threshold is reached.

iii. The length of the surgical procedure.
Estimates of the amount of fluid absorbed range from 10 – 30 mls per minute of resection time; over a 45 – 60 minute case that could equate to 1 – 1.8 litres.

Operation time; procedures that last longer than 60 minutes and those that require large amounts of tissue resection are more likely to lead to fluid volume overload. Theatre teams must have an established mechanism for measuring time and procedures for alerting surgeon and anaesthetist.

Recommendation 11
Operations should not last longer than 60 minutes. Theatre teams must have an established mechanism for measuring time and procedures for alerting surgeon and anaesthetist.

4.2.5 Theatre environment

A good theatre environment in terms of team dynamics is essential for the safe performance of these surgical procedures. There must be careful monitoring of fluid balance along with the clear communication of that balance to the surgical and anaesthetic members of the team.

- Theatre staff must always be aware of the potential hazards of, and equipment used, for any surgical procedure before it is performed.
- One core member of the theatre team must be assigned to the duty of gathering together the information needed to ensure the whole theatre team are aware of the distending fluid input & output and the deficit. They will need to be proficient and practiced in this technique and must not have other duties to perform while monitoring fluid balance. It would not be expected that the surgeon should have to operate and also supervise this function at the same time. They should remain in theatre for the duration of the procedure, in the same fashion as the surgeon.
- Medical staff must always have situational knowledge of the theatre environment that they are working in and the availability (or non-

availability) of any theatre equipment they consider necessary. They must be informed, in good time, of any equipment that is not working.
- Nursing staff should have a working knowledge of any equipment being used in their theatre or have the immediate presence of technical staff who do have that knowledge.

4.2.6 WHO checklist

Completion of the WHO surgical checklist with the sign in, time out and sign out must be adhered to. This will allow a surgical, anaesthetic and theatre team brief at the beginning for the whole theatre team and an opportunity to check that everything is in place to perform the biochemical and volumetric monitoring, to agree fluid absorption volume limits and should include discussion of limiting intravenous fluids intraoperatively.

It will also ensure at the sign out that any problems e.g. over a fluid deficit, are identified early. On a regional basis, adoption of a modified WHO checklist for this kind of procedure should be investigated and piloted.

Recommendation 12
Completion of the WHO surgical checklist must be adhered to. Adoption of a modified WHO checklist for this kind of procedure should be investigated and piloted.

5.0 IMPLEMENTATION OF POLICY

This policy, after it is agreed, is to be implemented throughout NI in each of the 5 Trusts.

5.1 Resources

There will be resource implications in terms providing surgical equipment that can be used without needing glycine as an irrigant, fluid flow and pressure controllers and POCT monitoring equipment for theatres and training for staff.

6.0 MONITORING

Trust audit departments will need to monitor that recommendations are implemented.

7.0 EVIDENCE BASE / REFERENCES

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8.0 CONSULTATION PROCESS

Consulted through the Medical Leaders Forum, DHSSPSNI and via the Medical Directors and Directors of Nursing.

9.0 APPENDICES / ATTACHMENTS

Appendix 1 = Suggested Theatre record form template.

10.0 EQUALITY STATEMENT

In line with duties under the equality legislation (Section 75 of the Northern Ireland Act 1998), Targeting Social Need Initiative, Disability discrimination and the Human Rights Act 1998, an initial screening exercise to ascertain if this policy should be subject to a full impact assessment has been carried out. The outcome of the Equality screening for this policy is:

Major impact ☐

Minor impact ☐

No impact. ☐

SIGNATORIES

_____ **Date:** _____

Author

_____ **Date:** _____

Director

Trust LOGO

Peri-operative fluid recording chart

Date: _____

Surgeon: _____

Anaesthetist: _____

Team Leader: _____

Circulating Nurse 1: _____

Circulating Nurse 2: _____

Addressograph Label

Fluid recorder: _____ Operation: _____

Fluid Medium: 3L 1.5% Glycine: ☐ 0.9% NaCl: ☐ Warmed: ☐

Bag Height: _____ mmHg ☐ (60 cms ≡ 50mmhg)

Preop. Serum Sodium: = _____ mmol/L Haemoglobin: _____ g/dL.

Resection: Start Time: _____:_____ Operation Finish Time: _____:_____

Irrigation fluid: Start time: _____:_____ **= 0 mins.**

Time (mins)	Irrigation In	Irrigation Out	Deficit	Running deficit	Serum Sodium	Surg. informed	Anaes. informed	Sign
5	mls	mls	mls	mls	mmol/L			
10	mls	mls	mls	mls	mmol/L			
15	mls	mls	mls	mls	mmol/L			
20	mls	mls	mls	mls	mmol/L			
25	mls	mls	mls	mls	mmol/L			
30	mls	mls	mls	mls	mmol/L			
35	mls	mls	mls	mls	mmol/L			
40	mls	mls	mls	mls	mmol/L			
45	mls	mls	mls	mls	mmol/L			
50	mls	mls	mls	mls	mmol/L			
55	mls	mls	mls	mls	mmol/L			
60	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			

Total Fluid In =	mls	Surgeon Signature	
Total Fluid Out =	mls	Anaesthetist Signature	
Total Deficit =	mls	Nurse Signature	
		Recovery Staff Signature	

Trust LOGO

Continued.

Time (mins)	Irrigation In	Irrigation Out	Deficit	Running deficit	Serum Sodium	Surg. informed	Anaes. informed	Sign
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			

Irrigation In	Document number of mls after each fluid bag is emptied. Record amount 'in' each time use Ellick evacuator.
Irrigation Out	Record fluid in • suction canisters. • fluid in drapes. • fluid from floor suction. Record amount 'out' each time use Ellick evacuator.
Deficit	Calculate deficit or record from pump readout.
Serum Sodium	Ensure there is a Serum Sodium measurement within one bold bordered box if procedure longer than 30 mins.

Glycine		
Volume Absorbed	**Effect**	**Action**
500 mls	Limit for the Elderly : comorbidities	Continue surgery
less than 1000 mls	Well tolerated by healthy patient	Continue Surgery
greater than 1000 mls	Mild hyponatraemia	Complete surgery ASAP
1500 mls	**Severe hyponatraemia & other biochemical disturbances likely**	**Stop Surgery**
Normal Saline		
2000 mls	Limit in the healthy	Complete surgery ASAP

Stinson, Emma M

From: Corrigan, Martina [Martina Corrigan's email address redacted]
Sent: 09 September 2015 13:29
To: Glackin, Anthony; Haynes, Mark; O'Brien, Aidan; ODonoghue, JohnP; Suresh, Ram; Young, Michael; Farnan, Turlough; Korda, Marian; Leyden, Peter; McCaul, David; Reddy, Ekambar; Hall, Sam; Ted McNaboe [Ted McNaboe's email address redacted]
Subject: FW: HSS(MD)14/2015 - POLICY ON THE SURGICAL MANAGEMENT OF ENDOSCOPIC TISSUE RESECTION
Attachments: HSS MD 14 2015 - POLICY ON THE SURGIVAL MANAGEMENT OF ENDOSCOPIC TISSUE RESECTION.pdf

FYI

Martina

Martina Corrigan
Head of ENT, Urology and Outpatients
Southern Health and Social Care Trust
Craigavon Area Hospital

Telephone: [Personal Information redacted by the USI]
Mobile: [Personal Information redacted by the USI]
Email: [Martina Corrigan's email address redacted]

From: Mackle, Eamon
Sent: 01 September 2015 13:11
To: Nelson, Amie; Reid, Trudy; Corrigan, Martina
Subject: FW: HSS(MD)14/2015 - POLICY ON THE SURGICAL MANAGEMENT OF ENDOSCOPIC TISSUE RESECTION

Dear All

Please forward to your consultants please

This mainly applies to Urology but may be relevant

Eamon

From: Medical Directors Office
Sent: 28 August 2015 10:23
To: Mackle, Eamon; Murphy, Philip
Cc: White, Sarah; Renney, Cathy
Subject: FW: HSS(MD)14/2015 - POLICY ON THE SURGICAL MANAGEMENT OF ENDOSCOPIC TISSUE RESECTION

Please cascade to all surgeons and physicians

Roisin

Roisin Feely
Medical Directorate Office
Clanrye House

Daisy Hill Hospital
☎: Personal Information redacted by the USI / DHH Ext. Personal Information
🖱: Personal Information redacted by the USI

From: Wright, Richard
Sent: 19 August 2015 11:10
To: Medical Directors Office
Subject: FW: HSS(MD)14/2015 - POLICY ON THE SURGICAL MANAGEMENT OF ENDOSCOPIC TISSUE RESECTION

For forwarding to all surgeons and physicians. Regards richard

From: Gordon, Lesley Lesley Gordon's email address
Sent: 18 August 2015 11:25
To: PA - Mr McCaughey; Dr Tony Stevens; Michael McBride; Mr Hugh McCaughey; Mr Liam McIvor (PS Joanne); Mrs Elaine Way; PA - Michael McBride; PA - Mrs Way; Wright, Elaine; PA - Tony Stevens; Clarke, Paula; Mairin McCann (PA); Valerie Watts (Chief Exec); Eddie Rooney; PA - Eddie Rooney; Dr David Stewart (Medical Director); Karen McCaffrey (David Stewart/Glenn Houston's Secretary); Mr Glenn Houston (Chief Executive)
Cc: David Bingham's email address Carolyn Harper; Hugh McKenna Dean of Life & Health Sciences H P McKenna's email address McArdle, Charlotte; Julian Johnston's email address Dr Cathy Jack; Dr David McManus; Dr Dermot Hughes; Dr Ken Lowry; Wright, Richard; Mr Charlie Martyn; PA - Dr Jack (Sharon); PA - Dr Lowry (Dorothy); PA - Dr McManus (Jane); White, Laura; PA - Mr Martyn (Alison); PA - Mr McKinney (Orlaith); Roisin Smith (Prof Elborne's PA); Angela McLernon (Interim Chief Executive); Keith Gardiner; Pauline Dardis; Dr Gavin Lavery; Dr Jackie McCall; PA to Drs Lavery/McCall; Alerts HSCB; Alerts PHA; Angela Dowds; Office, Coroners; Glynis Henry; Kevin Carland; Library (DHSSPS); MOD; Paul Gilliland; Paul Loughran; PC Intranet; Sean Keenan; Vincent Devine
Subject: HSS(MD)14/2015 – POLICY ON THE SURGICAL MANAGEMENT OF ENDOSCOPIC TISSUE RESECTION

Please see attached letter from Dr Paddy Woods, Deputy Chief Medical Officer and Mrs Charlotte McArdle, Chief Nursing Officer.

HSS(MD)14/2015 – POLICY ON THE SURGICAL MANAGEMENT OF ENDOSCOPIC TISSUE RESECTION

Many thanks

Lesley

Lesley Gordon
Personal Secretary to:
Dr P Woods (DCMO) & Dr A Kilgallen (DCMO)
Room C5.21
Castle Buildings
Stormont
BELFAST BT4 3SQ
Tel: Personal Information redacted by the USI
Fax: Personal Information redacted by the USI

MAKING LIFE BETTER

From the Deputy Chief Medical Officer
Dr Paddy Woods

HSS(MD)14 /2015

Department of
Health, Social Services and Public Safety
www.dhsspsni.gov.uk

Castle Buildings
Stormont
BELFAST
BT4 3SQ

Tel: Personal Information redacted by the USI
Fax: Personal Information redacted by the USI
Email: Personal Information redacted by the USI

Your Ref:
Our Ref: HSS(MD)14 /2015
Date: 18 August 2015

For Action:

Chief Executives HSC Trusts
Chief Executive HSCB
Chief Executive PHA
Chief Executive RQIA *(for dissemination to independent sector organisations)*

Dear Colleague

POLICY ON THE SURGICAL MANAGEMENT OF ENDOSCOPIC TISSUE RESECTION

ACTION REQUIRED

1. HSC Trusts and independent providers should process this regional policy template for endorsement by the organisational board, or equivalent;

2. HSC Trusts and independent providers should develop action plans to implement the various elements of the endorsed policy;

3. HSC Trusts should work with commissioners to address resource issues arising from these implementation plans in a phased, consistent and timely manner; and

4. the Public Health Agency should report on progress by 30 November 2015.

As a result of the verdict of the Coroner into the cause of death of Mrs Lynn Lewis in October 2013, work was commissioned on ensuring the safe and effective management of procedures involving the use of distending fluids in endoscopic procedures. In recognition of the limited guidance available on the management of these procedures, local work was commissioned, led by Dr Julian Johnston, Assistant Medical Director in Belfast Health and Social Care Trust.

The attached outline policy is the product of that work and we are now commending it for regional implementation.

The policy covers relevant issues including:

- appropriate preparation of patients prior to operation;
- selection of equipment and associated distending medium;
- precautionary measures associated with the distending medium selected;
- necessary measurements prior to, during and after these procedures;
- a good theatre environment in terms of team dynamics; and
- use of the WHO surgical checklist.

We believe this policy covers all aspects of concern raised by the Coroner in light of his findings in this tragic case.

We welcome your full assistance in this matter.

Yours sincerely

Dr Paddy Woods
Deputy Chief Medical Officer

Mrs Charlotte McArdle
Chief Nursing Officer

Cc HSC Trust Medical Directors
HSC Directors of Nursing Services
Chief Executive, BSO
Executive Medical Director/Director of Public Health PHA/HSCB
Dean Medical Faculty, QUB
Dean of Life and Health Sciences, UU
Chief Executive NIPEC
Chief Executive NIMDTA
Director of Safety Forum

This letter is available on the DHSSPS website at
www.dhsspsni.gov.uk/index/phealth/professional/cmo_communications.htm

Stinson, Emma M

From: Young, Michael <Personal Information redacted by the USI>
Sent: 12 October 2016 12:48
To: O'Brien, Aidan; Glackin, Anthony; Haynes, Mark; ODonoghue, JohnP; Corrigan, Martina
Subject: DeptMinutes 22 09 16 - saline resection
Attachments: DeptMinutes 22 09 16 - saline resection.docx; Saline resection Trial review and evaluation sept'16.docx

Please review document for sign off and final decision at next dept meeting

MY

DEPARTMENTAL MEETING 22nd SEPTEMBER 2016

Chair: Mr Young

Present: Mr Glackin, Mr O'Brien, Mr Suresh, Mr O'Donoghue, Pamela Johnston, Theatre Manager & Sr. England

Apologies: Mr Haynes , Mrs Corrigan

TOPIC: SALINE RESECTION

The specifications for the saline resectoscope system were presented. Mr Young outlined the history behind the move to the saline resection, also explaining that the last year had been spent trialling the various resectoscopes. Mr Young asked the forum if they had regarded enough time had been given to each of the resectoscope providing companies so that an adequate assessment could be made for each of the scopes. The unanimous decision was that the trial period for each of the resectoscopes was adequate to make an opinion.

We all agreed that the appraisal form used was of a good standard and certainly adequate to make a surgeons' assessment of each scope. The overall assessment looked at scope quality, ease of use, product design and effectiveness of the core principal of diathermy and resection of tissue. Second component to be evaluated were costs of generators and disposables. Thirdly was the topic of CSSD and backup. Scoring was undertaken from the feedback forms with the result that the WOLF system was the poorest and was not fit for purchase. In third place was the TONTARRA system which was described as having a variable performance with regards to the resection loop activity. The STORZ and the OLYMPUS system scored virtually equally on the various points with an overall equal score. It was recorded that there was no cystoscope present on the OLYMPUS resectoscope tray for evaluation but we generally felt that this was not an issue to take into account. There was general record of a fairly good ease of use and that the vaporisation module component was good. Several negative points related to the working element of inflow/outflow not being ideal; there were some comments on excessive bubble formation on the resectoscope loop as well as some other comments relating to slow resection. Overall however this was a system that could be purchased. With regards to the STORZS system, it was felt that the cutting modality of the resectoscope loop was excellent. Overall the scope components were easily constructed and there was a generalised good ease of use. Comments with regards to consistency and haemostasis had been positive. One of the major points in its favour was that the STORZ system could be easily changed if required on an urgent basis to the use of glycine. This in the current climate of change from one system to another in association with the range of urologists within the unit was a more suitable system for the team in Craigavon Area Hospital. The STORZ system certainly was a system that could be purchased.

Purely on the ease of use principal, excluding other criteria (i.e. cost and CSSD), the option came down to either STORZ or the OLYMPUS system, the other two being excluded. Four surgeons voted for the STORZ, one electing for the OLYMPUS. Mr Haynes was not present for this vote but on subsequent conversation later in the day, Mr Young put the same question to Mr Haynes asking for his comments on ease of use and again he had no particular preference and was happy to run with the global opinion.

On reviewing the various costs, it was noted that the disposables did have a variable range. It was accepted that loop quality did vary and that loops could be purchased from different sources. We all felt that this was not a particularly focused point for making a decision (namely cost of loop).

The price of the individual resectoscope systems was recorded noting that the OLYMPUS system was significantly more expensive in totality. The OLYMPUS system would have to be purchased completely whereas the STORZ system could be involve both new scopes and modification of current sets. (The costs set out for this meeting were significantly in favour of the STORZ system but it was appreciated that if a STORZ completely new systems was to be included that this information was to be presented to the forum before a final decision was made).

A further significant contributor to decision making was the generator needed for the electrical input. Although the OLYMPUS company was going to offer a free £40,000 generator, we did record that we may need up to three generators in view of the amount of urology sessions occurring at the same time. (The forum did not know if the company would supply three free generators. They felt it unlikely but enquiries would be made). The current generator system available within the Trust is multifunctional and therefore would already suit the STORZ system more appropriately. Even with the OLYMPUS generator system, this would result in increased machinery parking within the theatre environment. Overall this was regarded as a fairly substantive pointer in favour of the STORZ system.

CONCLUSION

In concluding, the vote on several aspects namely ease of use, cost, generator type were all in favour of the STORZ system. All the urologists have backed this decision with a unanimous vote.

This decision was based on the information supplied with a final decision pending the outstanding enquiries, namely the cost of a completely new STORZ resectoscope system and the cost of the OLYMPUS cystoscope. This would give a truly like for like comparison. The additional enquiry related to the OLYMPUS generator issue.

Mr Young will add an addendum to this document when the above information becomes available before final sign off.

The paperwork with regards to this has been forwarded to the Service Administrator, Martina Corrigan and to Pamela Johnston, Theatre Manager.

M Young
22nd September 2016
Chair of Session

ADDENDUDEM to outstanding information in relation to Saline resection Systems

1/ Full cost specification for STORZ and OLYMPUS resectoscope systems (excluding generator) have now been supplied and presented by the Theatre management. This is included on the updated evaluation sheet. (see enclose document)

(*The conclusion of the forum group remains the same – namely that STORZ is less expensive*)

2/ OLYMPUS will only supply one free generator

This information is to be presented at the next Departmental meeting for ratification

M Young

12th October 2016

Saline Resection Trial evaluation- Date: 15th Sept'16 Review

Selection Criteria	Storz	Wolf	Olympus	Tontarra	Comments
Ease of Use: Quality and Design and ease of use with active resecting mechanism	**Score 45**	30*	44	38	*Wolf rep unavailable to support trial with generator. No extra electrodes sent for trial despite requests- company sent incorrect electrode
Fit for Purpose: • Continuous Flow System	**44**	25	44 *	34	*Olympus did not have cystoscope available on tray for trial
Product Quality: Loop and Ball Electrode ○ Quality and Design and ease of use ○ Precision of Cut	**45**	27	45	33	Tontarra- reusable breakages (single use electrode now available)
Overall performance	**43**	24	44	35	
TOTAL	**177**	106	177	140	

Received from Mark Haynes on 03/11/2023. Annotated by the Urology Services Inquiry.

Selection Criteria	Storz	Wolf	Olympus	Tontarra	Comments
Cost: Bi-Polar Resection Kit	**£2006.69**	£4925	£8575.65	**£4880 (Trade in £4000)**	• Storz- only need lead and resect scope (kit items required telescope/working element, continuous flow sheath, obturator, view obturator, light guide, bipolar cable, basket)
Consumables- per loop electrode **Coagulation ball**	**£47.50** **£47.50**	£77 £71	£126.66 £156.66	£53 £53	Updated 15/
Generator	**Not required- Erbe/Covidien compatible**	**Erbie with Booster * Costs not**	Free of cost £40,000 (approx.)	**Not required- Erbe/Covidien compatible**	

		supplied			
Support and Service a. Responsiveness b. Training	**Good-** support for each day of trail	**Poor-** limited support	**Fair-** inexperienced rep	**Good-** regular rep support and good knowledge	
CSSD Comments:	**No issues**	**No issues**	**No issues**	**No issues**	**No issues**
Urology Consultants preference 1-4 Rationale 15/9/16					

Specification Required for Saline Resection Trial evaluation

2. Resection using Saline irrigation

3. Continuous Flow System

4. Quality and Design and ease of use with active resecting mechanism

5. Disposable/Reusable Loop and Ball Electrode
    a. Quality and Design and ease of use
    b. Precision of Cut

6. Dual foot pedal

7. Support and Service
    a. Responsiveness
    b. Training

8. CSSD Issue - Sterilisation Process

9. NHS Framework

10. COST: Equipment and Consumables (Based on average 300 cases per year)

11. Service Contracts

Received from Mark Haynes on 03/11/2023. Annotated by the Urology Services Inquiry.

Stinson, Emma M

From: Haynes, Mark [Mark Haynes's email address]
Sent: 17 November 2017 06:28
To: Corrigan, Martina
Subject: RE: saline TURP issue

I'll bring up with Richard separately.

Can you forward me the Findings / recommendations of the review?

Mark

From: Corrigan, Martina
Sent: 16 November 2017 20:15
To: Haynes, Mark
Subject: Fw: saline TURP issue

As discussed

Martina

Martina Corrigan
Head of ENT, Urology, Ophthalmology and Outpatients
Craigavon Area Hospital

Office: [Personal Information redacted by the USI]
Mobile : [Personal Information redacted by the USI]

From: Young, Michael [Michael Young's email address]
Sent: Thursday, 16 November 2017 17:55
To: Carroll, Ronan
Cc: Corrigan, Martina
Subject: saline TURP issue

Dear Ronan
I write with regards to the saline TURP issue.
As you are aware the DoH had undertaken a review of irrigation fluid used for TURP surgery a few years ago after a significant adverse event in which a young lady died. As a result a clearly documented pathway noted that hospitals in Northern Ireland should move to using saline as opposed to glycine for irrigation. In the Southern Trust we have been using glycine and therefore it has been necessary for us to convert over to new equipment for our Consultants and team to be compatible with DoH guidelines.

Several saline resectoscope systems are available. We have proceeded through a process of trialling each of these. We have considered several factors, including efficiency of use through to the financial impact, before coming to a conclusion. We as a department felt this was important to undertake as there would be long term implication to our decision. In saying all of this, we still felt that a defined date to transfer over to the new system was needed. We defined this date as 1st January 2018. This date was defined as fitting a timeline that allowed for the trail period, quotes to be received, assessment and providing the Trust a reasonable period of time to purchase the equipment.

The move to using Saline for TURP resection has been dictated by the DoH. The consequences of not moving to its use will leave Consultant Urologists at risk as if another significant adverse incident occurs they will feel very much

exposed. I am not sure the Southern Trust would be able to cover them properly if such an event occurred when it is clear the DoH had made their stipulation.

We were under the distinct impression that having gone through our selection process and giving adequate notice, as discussed at the Theatre Users group, that this date was reasonable and would be compliant with the DoH documentation and hence for the Trust to be able to report back to DoH on the same.

It has now come to my attention that the Trust is not able to or in a position to proceed with the purchase of this equipment. It is not clear why this is the case as we have been instructed to move over to this system by the Trust itself.

Urologists in the department will be maintaining their position for a switch to using saline to perform TURP as of 1st January 2018. If the new equipment is not available the Urologists will cease the current type of TURP surgery. I am sorry this appears a little dogmatic, but the DoH and Coroners case that has sparked this course has been clearly set out and leave Consultants vulnerable if they do not attempt to comply.

M Young
Lead Clinician Urology

Stinson, Emma M

From: john mcknight [redacted]
Sent: 28 May 2015 17:26
To: Brian Duggan; [redacted] Sam Gray; [redacted] colin mulholland; [redacted] Trevor thompson; hugh o' kane; alex macleod; ajay pahuja; p keane; david connolly; chris hagan; ODonoghue, JohnP; Haynes, Mark; Ali Al-Inizi; siobhan woolsey
Subject: FW: Endoscopic Distending fluids for the Coroner
Attachments: Letter from Mr Leckey re L Lewis 21 10 13.pdf; Policy on surgery for endoscopic tissue resection V0.4.docx; NICE 2015 - The TURis system for transurethral resection of prostate.pdf

Attached is email form J Johnston re TUR.

I think all agree that there should be a move towards TURis for prostates. Previous discussions suggest that many would like to still have the ability to use glycine for TURPs as a back up. The complication profile for TURP in the literature used to support the NICE application is interesting.

More concerning is the extrapolation to use for TURB, which is un-evidenced and not standard practice. Informal discussions with BAUS section of Oncology are not aware of any significant reason to recommend such a change.

The gynae change is unchallenged.

If a clear picture of concern is not again fed back, the current document will be seen as a final document and will see glycine removed or at best see those that use it for bladder tumours or prostates it as unsupported.

I would be grateful if all would reply to me with there current position of TURis for both prostates and bladder tumours, with or without retention of ability to use glycine. Or if there is any other comment about this issue.

John

John McKnight
Belfast N.Ireland
Mob [redacted]

From: [redacted]
To: [redacted]

Subject: RE: Endoscopic Distending fluids for the Coroner
Date: Tue, 26 May 2015 16:41:46 +0000

Distending Fluids for Endoscopic surgery
Please find attached my final document with 12 recommendations which I propose represents the required 'collegiate ' response to the failings surrounding the death in the UIC. This is in response to the Coroner asking the CMO that 'the Medical Directors to provide me with a collegiate response to the surgical and anaesthetic failings that the inquest has identified and ... similar response from the NI CNO in relation to nursing issues'.

I presented draft work at 2 recent Medical Leader Forums. After the last one I received further feedback regionally. Thank you to those who sent in comments to the draft policy for Distending Fluids for Endoscopic surgery. I have responded to those who sent in comments with a further amended document.

Other important changes have followed the publication, in February 2015, of a NICE Medical Technology Guidance note 23 where they 'point out at the case for adopting the transurethral resection in saline (TURis) system for resection of the prostate is supported by the evidence'. Furthermore they also provide similar advice to the public http://www.nice.org.uk/guidance/mtg23/informationforpublic. I regard this work by NICE as a very potent argument for proceeding in the direction I propose.

I have taken account of the comments from the region and incorporated them, along with the guidance from NICE, into this final document.

I am content now that this does represent a majority view from around the Province. Please share this with your colleagues if they are not on the list above.

I have now shared this with the DHSSPSNI and all the Medical Directors.

Regards,

Julian R Johnston MD FCARCSI FRCA
Assistant Medical Director
BHSCT
Julian Johnston's email address

BHSCT Litigation Management Office
Telephone: Personal Information redacted by the USI
If unanswered, contact Ann Maginnis: Personal Information redacted by the USI or Amanda Lennon (Coroner's Office): Personal Information redacted by the USI or Susan McCombe (Clinical Negligence): Personal Information redacted by the USI or Lorraine Watson (BCH Clin. Neg./Coroner's) Personal Information redacted by the USI .

From: Johnston, Julian
Sent: 27 February 2015 16:58
To: Michael Young's email address 'McKnight, John'; 'McAllister, Charlie'; Hagan, Chris; 'Darling, John'; David Morgan's email address David Glenn's email address D Glenn's email address Geoff McCracken's email address Michael Parker's email address Colin Pendergast's email address McClelland, Raymond; Keith Johnston's email address Gary Dorman's email address John J McKnight's email address

Cc: 'Simpson, John'; 'Alan McKinney [redacted] Jack, Cathy; [redacted]

Subject: Endoscopic Distending fluids

Please attached a second draft policy setting out a proposed collegiate view for managing endoscopic tissue resection.
I have taken into account views expressed to me following the first time I sent out a draft policy.
I have also examined in detail the recent literature and documents from NICE and the Cochrane Collaboration.
This document has been substantially modified and forms the basis of presentations to the Medical Leaders Forum.

It details a direct of travel. My inquiries and those of leaders in urology and gynaecology indicate that there is now support for what is described.
If a sizeable majority of urologists and gynaecologists are in agreement, then that will be the direction proposed to the Trusts MDs and the CMO.

I would like views expressed to me by 15th March 2015 please.
Please circulate this to interested colleagues who are not on the email list above. I think I am missing the names of some Urologists.

Regards,

Julian R Johnston MD FCARCSI FRCA
Assistant Medical Director
BHSCT
[redacted]

Co-Chair Standards and Guidelines Committee
Standards, Quality and Audit department
Telephone: [redacted]
If unanswered, contact Christine Murphy : [redacted] or Jill Shaw O'Doherty : [redacted] or Simon Dunlop : [redacted]

BHSCT Litigation Management Office
Telephone: [redacted]
If unanswered, contact Ann Maginnis: [redacted] or Amanda Lennon (Coroner's Office): [redacted] or Susan McCombe (Clinical Negligence): [redacted] or Lorraine Watson (BCH Clin. Neg./Coroner's) [redacted].

Coroners Service for Northern Ireland

JOHN L LECKEY LL.M.
SENIOR CORONER
FOR NORTHERN IRELAND

Dr Tony Stevens, Medica Director, BHSCT
Dr Charlie Martin, Medical Director, SEHSCT
Dr John Simpson, Medical Director, SHSCT
Dr Alan McKinney, Medical Director, WHSCT
Dr Calum MacLeod, Medical Director, NHSCT
Dr Carolyn Harper, Executive/Medical Director of Public Health
Ms Charlotte McArdle, Chief Nursing Officer

HSC Belfast Health and Social Care Trust
25 OCT 2013

Our ref: 1791-2011

21st October 2013

Dear Medical Director
and Chief Nursing Officer,

Re: Lynn Lewis, deceased

On 16th October 2013 I concluded an inquest into the death of a 38 year old woman, Mrs Lynn Lewis, who died in the Ulster Independent Clinic on 7th July 2011.

I believe sufficient background information is contained in the Verdict to which is annexed a copy of a statement on behalf of Professor Neil McClure the Surgeon, Dr Damien Hughes the Anaesthetist, the Ulster Independent Clinic and the nursing staff (copies enclosed). Also, I am enclosing a copy of a letter I have sent to the Minister for Health together with copies of the enclosures therein referred to.

At the conclusion of the inquest I stated that in addition to making a report pursuant to the provisions of Rule 23(2) of the 1963 Coroners Rules to the Minister, the Chief Medical Officer, the Regulation and Quality Improvement Authority and the Director of Public Health I would be writing to the Medical Director of all Northern Ireland Hospitals and the Northern Ireland Chief Nursing Officer. I would ask the Medical Directors to provide me with a collegiate response to the surgical and anaesthetic failings that the inquest has identified and I would ask for a similar response from the Northern Ireland Chief Nursing Officer in relation to nursing issues.

I should be grateful if you would acknowledge receipt of this letter and confirm that you will be responding in the manner I have requested. I, and no doubt the family also, require reassurance that all steps have been taken to ensure patient safety and

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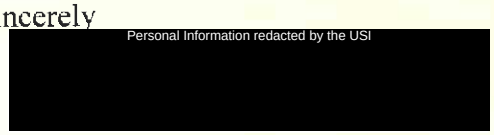
www.coronersni.gov.uk

everything possible has been done or will be done to prevent the occurrence of a similar fatality or other serious adverse incident that has not resulted in a fatality.

I am sending a copy of this letter to the Minister, CMO, RQIA, Director of Public Health and the legal representatives.

I will look forward to hearing from you.

Yours sincerely



J L LECKEY
Senior Coroner for Northern Ireland

Encs

Trust LOGO

Reference No:

Title:	Policy on the surgical management of endoscopic tissue resection, for example during urological, gynaecological and other relevant surgery.			
Author(s)	List name and titles of lead and additional author(s) or group responsible for drafting policy Include contact details			
Ownership:	Insert name of Director / service area / group / directorate			
Approval by:	Insert name of Trust committee / group responsible for approval		**Approval date:**	Insert date each committee approved
Operational Date:	May 2015		**Next Review:**	May 2017
Version No.	V0.4	**Supercedes**	Any legacy policies.	
Key words:	Endoscopic, Resection, Prostatectomy, Myomectomy, TUR syndrome			
Links to other policies				

Date	Version	Author	Comments
20/11/2013	0.1	SE Trust	Initial Draft
03/12/2013	0.2	JR Johnston	Amalgamation of protocols from 5 Trusts.
01/02/2015	0.3	JRJ	Following 3/11/14, 19/01/2015 MLF meetings
20/03/2015	0.4	JRJ	Following regional feedback, NICE publication

Recommendations

This policy sets out a regional co-ordinated 'collegiate' improvement programme for surgical endoscopic tissue resection, with,

- a plan to use the safest resection technique currently available with its attendant irrigation fluid.
- establishing a set of safe practice standards and set of precautions to minimise the risk of intravascular absorption.

1. Preoperative workup **must** be geared towards prevention of the TUR syndrome.
2. Introduce Bipolar equipment using saline, regionally; curtail the use of glycine as a irrigant, strictly monitor when it is still used and eventually stop when there ceases to be circumstances when glycine use is considered the safest.
3. Engineer changes in the type of procedures performed.
    a. More secondary procedures for management of heavy menstrual bleeding as per NICE recommendations.
4. Increase vigilance when significant haemorrhage is a feature.
5. If continue to use glycine, the following **MUST** be used,
    a. Measure POCT serum sodium,
        i. preoperatively.
        ii. if the surgery is longer than 30 minutes as a routine.
        iii. intermittently throughout the surgery.
        iv. if there is a 1000 ml fluid deficit.
    b. Dedicated staff for transporting specimens and results.
    c. Surgery, including TURP, TCRE & TCRF must be performed in a 'main' theatre where POCT equipment is immediately available.
6. Limiting the distension pressure by,
    a. maintaining it below the mean arterial pressure (MAP).
    b. attempting to limit the height of the irrigating solution container to 60 cm above the patient and certainly never above 100cm.
    c. Theatre teams must have a procedure for checking and maintaining an agreed height.
    d. not applying pressure bags to the irrigation fluid bag.
7. Investigate instilling irrigation fluid by using a pressure controlled pump device and purchasing flow/pressure controllers.
8. The theatre team **must**,
    a. be aware of the distending fluid input & output and deficit.
    b. contain a dedicated nurse for fluid balance and deficit calculation, who remains in theatre for the duration of the procedure.
9. If continue to use glycine, the following **MUST** be used, throughout the procedure,
    a. Accurate irrigation fluid input & output measurement and deficit calculation.
10. Preoperatively, there **must** be an agreed maximum fluid deficit threshold for action. The surgeon and anaesthetist **must** be informed by the nurse when the threshold is reached.
11. Operations should not last longer than 60 minutes
    a. Theatre teams **must** have an established mechanism for measuring time and procedures for alerting surgeon and anaesthetist.
12. Completion of the WHO surgical checklist **must** be adhered to. Adoption of a modified WHO checklist for this kind of procedure should be investigated and piloted.

1.0 INTRODUCTION / PURPOSE OF POLICY

1.1 Background

Some endoscopic surgical procedures require the use of an irrigating fluid to distend the operating field to enable a suitable field of vision and to wash away debris and blood. This includes operations such as,

- resection of prostate (TURP) and bladder tumours (TURBT).
- transcervical resection of endometrium (TCRE), transcervical resection of fibroids (TCRF).
- removal of uterine septum, polyps, endometrial ablations.
- cystoscopy, arthroscopy, rectal tumour surgery, vesical ultrasonic lithotripsy and percutaneous nephrolithotripsy.

Endoscopic operations where there is tissue resection can lead to serious complications such as haemorrhage, fluid overload, hyponatraemia, cerebral oedema and death. This policy concentrates on a subset of these; the transurethral resection (TUR) syndrome[1], when systemic intravascular absorption of irrigation fluid can cause serious symptoms.

This policy sets out the steps needed to improve the safety profile of this type of surgery. Using national policies, guidelines and evidence identified in section 7 along with on-going work within the province, its aim is to establish a regional 'collegiate' improvement strategy for all surgical (urology, gynaecology) teams in NI practicing this type of surgery to,

- use the safest resection technique with its attendant irrigation fluid.
- agree a programme of change for the cessation of glycine use.
- develop or adopt techniques that do not rely on glycine as an irrigant.
- use equipment designed to control or reduce vesical or uterine pressure.
- establish a set of safe practice standards and precautions to minimise the risk of intravascular absorption.

Some of the recommendations can be instituted now and some will depend on the financing of equipment.

1.2 Irrigation fluids used

The irrigation fluid used for these electrosurgical procedures should,

- have neutral visual density so that the surgeon's view is not distorted.
- be non-haemolytic and will not lead to haemolysis if it enters the circulation.

Until relatively recently, the standard equipment used to resect tissue was of a **monopolar electrode** design which requires an electrically nonconductive irrigating fluid so the electrical current is not dissipated and can remain concentrated at the cutting point. As described below, use of this type of fluid bears the risk of the TUR syndrome.

Recently introduced **bipolar resection equipment** is different to the monopolar type in that it incorporates both active and return poles on the same electrode. This allows a conductive fluid medium (normal saline) to be

used for the irrigating fluid instead of a 'conventional' nonconductive irrigation fluid (glycine, sorbitol or mannitol).

Irrigating fluids
In the past, **sterile water** was used as the irrigant but was associated with significant morbidity because of water intoxication and intravascular haemolysis.

Modern non-electrolytic solutions containing glycine 1.5%, mannitol or sorbitol are optically clear and were introduced to prevent haemolysis, without dispersing the electric current used for cutting with the resectoscope. Their use in irrigation solutions has reduced the occurrence of significant haemolysis and death.

The most commonly used irrigation fluid has been 1.5 % **glycine solution,** a non-essential amino acid with a low cost and lack of allergic reactions**.** However, it has an osmolality of 200 $mOsm.kg^{-1}$ which is much lower than that of blood [Plasma = 290 $mosmol.kg^{-1}$] and large amounts of this hypotonic irrigation fluid, required to facilitate the procedure, may be absorbed systemically through a vascular bed[2]. This may cause several serious complications known as the **TUR syndrome** which can occur in a variety of surgical disciplines.

Normal saline is used for irrigation with the bipolar resectoscope. It is associated with fewer unfavorable changes in serum sodium and osmolality than is the case when electrolyte-free media are used with monopolar systems[3] e.g. glycine. Its use, however, does not eliminate the need to prevent excess absorption or to closely monitor fluid balance, as overload can occur. Pulmonary oedema is a reported consequence.

1.3 TUR syndrome[4]

The transurethral resection (TUR) syndrome is an iatrogenic form of acute water intoxication from a combination of fluid overload and hyponatraemia. While first recognised in urology, hence its name, it can occur in other surgical specialties e.g. gynaecology.

It is manifested mainly through a classic triad of,

- fluid overload - acute changes in intravascular volume leading to circulatory overload, pulmonary oedema, cardiac failure and even cardiac arrest.
- dilutional hyponatraemia causing central nervous system (CNS) effects such as cerebral edema leading to agitation, confusion, convulsions and coma.
- direct toxicity and metabolism of glycine which may also cause CNS symptoms, most commonly transient blindness and CNS depression, as it is an inhibitory neurotransmitter. Its metabolism yields water (worsening fluid overload) and ammonia.

The incidence of TUR syndrome for TURP appears to have reduced over the last two decades with recent studies demonstrating incidence rates of 0.8% -

1.4%. The occurrence of the TUR syndrome following bladder tumour resection (TURBT) is thought to be rarer but can occur, probably via either an intraperitoneal or extraperitoneal bladder perforation.

There is a observation that the incidence and effects of this syndrome are more pronounced in gynaecological than in urological surgery. Fluid absorption is slightly more common during TCRE than during TURP, with transcervical resection of fibroids (TCRF) being at a further increased risk over TCRE. Whereas hyponatraemia occurs with equal frequency in men and women, it is more likely to produce severe complications in premenopausal women[3]. Nevertheless, the necessity to constantly seek best and safest practice and to encourage change and improvement is the same for both specialties.

1.4 Purpose

This policy outlines a set of principles designed to reduce the development of the TUR syndrome.

1.5 Objectives

To reduce the likelihood of developing the TUR syndrome through,

- correct patient selection and preoperative preparation.
- selection of an appropriate surgical technique.
- electing to use surgical equipment which allows the use of irrigation fluid which will not give rise to the TUR syndrome.
- the application of monitoring aimed at detecting the early warning signs of the TUR syndrome.
- establishing a theatre regime based on good theatre practice principles aimed at reducing the development of the TUR syndrome.

2.0 SCOPE OF THE POLICY

This policy applies to all staff who may be involved in the care of a patient in theatre who receives irrigating fluid into the bladder or uterus or any other organ where significant fluid absorption is a realistic possibility.

It applies to medical staff, nursing staff, midwives, operating department practitioners, technical staff, physicians' assistants (anaesthesia) and other theatre healthcare workers.

This policy does not cover the methods of treatment of the TUR syndrome.

3.0 ROLES/RESPONSIBILITIES

Medical staff to,

- ensure they are fully cognisant of the risks of the TUR syndrome.
- undertake careful consideration of the therapeutic choices when planning the service for endoscopic resection in order to reduce the likelihood of the development of the TUR syndrome.

Management – actively supporting the introduction of therapeutic modalities that aim to reduce the incidence of the TUR syndrome.

All staff involved in the care of the patient, especially in theatre, are responsible for implementing and adhering to the policy principles.

Each ward/theatre sister/charge nurse/clinician involved with this kind of surgery is responsible for ensuring staff comply with this policy and all relevant staff have the responsibility to ensure that they read and comply with the policy contents.

In the event of an untoward incident an adverse incident form must be completed by either the medical officer or nurse in charge of the patient's care.

4.0 POLICY PRINCIPLES

4.1 Definitions

Osmolality: The concentration of osmotically active particles in a solution.

Hypertonic: Higher osmolality (concentration of particles) than that found in normal cells.

Hypotonic (or hypo-osmolar): Lower osmolality (concentration of particles) than that is found in normal cells.

Hyponatraemia: Lower sodium concentration than normally found in plasma.

Resectoscope: An endoluminal surgical device comprising an endoscope (hysteroscope or cystoscope), sheaths for inflow and outflow, and an ‘‘element’’ that interfaces a specially designed electrode (or pair of electrodes) with a radiofrequency (RF) electrosurgical generator which can be either monopolar or bipolar.

4.2 Policy Principles

An irrigating fluid is most frequently absorbed directly into the vascular system when a vein has been severed by electrosurgery. The driving force is the fluid pressure; the volume of fluid absorbed depending on the,

- duration of the procedure and resection time,
- degree of opening of blood vessels during surgery,
    - vascularity of the diseased prostate, uterus, fibroid.
    - surgical disruption of the bladder, uterine vessels.
    - capsular or uterine wall perforation or apparent damage to a venous sinus.
- pressure of the distending fluid within the bladder or uterus,
    - height of the irrigation fluid bag above the patient.
    - distension pressure applied to the irrigation fluid.

For safe endoscopic resection using irrigation fluid, consideration of the following topics needs covered,

a. Preoperative workup.
b. Selection of surgical technique.
c. Identification, control and management of haemorrhage.

d. Control of the absorption of irrigation fluid.
    a. Dilutional Hyponatraemia.
    b. Fluid overload.
    c. Glycine toxicity.
e. Theatre environment.
    a. Decision making processes.
    b. Team dynamics.
    c. Knowledge of potential complications.

4.2.1 Preoperative workup

Careful preoperative workup of the patient must include, for example,

- a robust consent process leading to a truly informed patient aware of the hazards of endoscopic resection using irrigation fluids.
- a thorough physiological assessment with attention paid to risk factors such as hypertension, ischaemic heart disease, cardiac failure, anaemia.
- standard haematology and electrolyte analysis - to include a recent haemoglobin, serum sodium.
- careful consideration regarding blood grouping and cross-matching.
- recent investigations aimed at establishing the pathological anatomy and degree of surgical risk especially haemorrhage e.g. ultrasound scan.
- the ready availability of reports of such investigations before surgery commences.

Recommendation 1
Preoperative workup **must** be geared towards prevention of the TUR syndrome.

Urology

These procedures are carried out on a predominantly elderly population with a high incidence of coexisting disease. BPH affects 50% of males at 60 years and 90% of 85-year-olds and so TURP is most commonly performed on elderly patients, a population group with a high incidence of cardiac, respiratory and renal disease.

Gynaecology

Consideration should be given to the timely commencement of any adjuvant therapy prior to the surgery[3], especially if it helps to reduce the risk of haemorrhage and/or causes a reduction in tumour size.

4.2.2 Selection of surgical technique

Urology

Absorption in excess of 1 litre of glycine solution, which is associated with a statistically increased risk of symptoms, has been reported in 5–20% of the TURPs performed[1].

One of the most important recent improvements in this field has been the introduction of bipolar electrode technology (B-TURP). This addresses the

fundamental flaw of monopolar equipment (M-TURP) by allowing resection in a normal saline irrigation. Therefore, the adoption of bipolar TURP/TURBT allows NS irrigation and permits the removal of glycine and its inherent risks from theatre. The risks of the hyponatraemic and hypo-osmolar aspects of the TUR syndrome are eliminated.

There are several manufacturers who have developed bipolar endoscopy systems. Early local adopters of this type of equipment have experience of several of them and have observed a progressive and continuing development cycle which has now resulted in really excellent systems. They also observe that some other manufacturers have not kept pace. It is important that views on the performance of these bipolar systems are based on the most modern examples and on those manufacturers who have managed to develop the most efficient systems.

B-TURP is the most widely and thoroughly investigated alternative to M-TURP[5]. There is now increasing recent evidence[6 - 9] for the effectiveness of bipolar systems as their technical performance has been developed and improved. Indeed there is some evidence[9] that bipolar may be better at improving urine flow rates and also reducing bleeding related complications as well as eradicating the TUR syndrome. With reduced bleeding and improved visibility, resection time can be decreased.

Moreover, recent systematic reviews[7, 9] are not only repeatedly describing equal effectiveness between monopolar and bipolar techniques but are also pointing out the significantly improved safety profile for bipolar.

Significantly, the TUR syndrome has not been reported with bipolar equipment[5]. A recent systematic review and meta-analysis[9] comparing traditional monopolar TURP with bipolar TURP established in 22 trials that the TUR syndrome was reported in 35/1375 patients undergoing M-TURP and in none of the 1401 patients undergoing B-TURP. Even taking into account that one study alone was responsible for 17 of the 35 cases, the accompanying editorial states, "*the elimination of TUR syndrome alone has been a worthy consequence of adopting bipolar technology."*

This is supported by recommendations within the European Association of Urology guidelines[5] on TURP management of April 2014. "*B-TURP has a more favourable peri-operative safety profile compared with M-TURP."*

In 2012, NICE recommended[10] that bipolar techniques are associated with lower rates of complications and in October 2014 they opened up support[11] for the use of transurethral resection in saline which eliminates the TUR syndrome and may also reduce length of stay as well as having cost benefits.

In February 2015, they published their medical technology guidance[12] on a transurethral resection in saline system. They point out that the case for adopting the transurethral resection in saline (TURis) system for resection of the prostate is supported by the evidence.

They also indicate that,

- the TURis system can be used instead of a surgical system called ‘monopolar transurethral resection of the prostate’ (or monopolar TURP).
- Healthcare teams may want to use the TURis system instead of monopolar TURP because:
    - there is no risk of a rare complication called transurethral resection syndrome.
    - it is less likely that a blood transfusion after surgery will be needed.

NICE used an External Assessment Centre to analyse the clinical evidence and concluded that their meta-analysis found a statistically significant effect in favour of TURis: relative risk 0.18 (95% CI 0.05 to 0.62, p=0.006), corresponding to a number needed to treat to prevent 1 case of TUR syndrome compared with monopolar TURP of 50 patients.

The External Assessment Centre did not identify any special additional training needs for a switch to the TURis system from monopolar transurethral resection of the prostate (TURP). The NICE Committee received expert advice that confirmed that little training is needed for surgeons who are already performing monopolar TURP procedures.

The sources of evidence considered by the NICE committee included expert personal views from at least 5 clinical experts from the British Association of Urological Surgeons (BAUS).

NICE, in February 2015, also issued guidance for the public on this topic. They indicated that, “*the TURis system can be used instead of a surgical system called ‘monopolar transurethral resection of the prostate’. Healthcare teams may want to use the TURis system instead of monopolar TURP because there is no risk of a rare complication called transurethral resection syndrome and it is less likely that a blood transfusion after surgery will be needed.”*

Therefore, the case for moving from a monopolar to bipolar technique for resection of the prostate would appear to be well established as safer with regard to the development of the TUR syndrome. However, it should be remembered that the use of NS is not without risk because there will still be fluid absorption with plasma volume expansion.

Also, queries have been expressed over a potential degradation of pathological specimens with the use of this new technology which might have staging implications for bladder tumour management. However, the experience of both surgical and pathology staff within the BHSCT has been that they have not noticed any major difference. There is also no evidence based literature to support the view that bipolar resection causes any more damage and in fact the incidence of severe cautery artefact was significantly lower in the bipolar resections[13], a view subsequently supported in an accompanying editorial[14] which also exhorts, “*as urologists we have shown again and again that we are quick to adopt new technologies in routine practice*”.

Therefore (as long as they are proven to be safe and effective as judged by the NICE interventional procedure programme), bipolar RF systems and other techniques e.g. laser systems, should be introduced regionally. By introducing the, as effective, but safer bipolar equipment, this should, by necessity, reduce and curtail the use of glycine as a irrigant. Its continuing use should be strictly monitored and eventually terminated when there ceases to be circumstances when its use is considered the safest.

Recommendation 2
Introduce Bipolar equipment using saline, regionally; curtail the use of glycine as a irrigant, strictly monitor when it is still used and eventually stop when there ceases to be circumstances when glycine use is considered the safest.

Gynaecology

The first generation endometrial ablative techniques including transcervical resection of endometrium (TCRE) and rollerball endometrial ablation (REA) are all endoscopic procedures. Fluid absorption is slightly more common during TCRE than during TURP, with transcervical resection of fibroids (TCRF) being at a further increased risk over TCRE. As TCRE often evolves into a TCRF when fibroids are found during hysteroscopy, it means the same safety procedures need to be put into place for both TCRE and TCRF.

Their effectiveness in the management of heavy menstrual bleeding (in comparison with hysterectomy - the existing gold standard) has been demonstrated in a number of randomised controlled trials. Although less morbid than hysterectomy, they are associated with a number of complications including uterine perforation, cervical laceration, false passage creation, haemorrhage, sepsis and bowel injury and, importantly, the fluid overload and hyponatraemia associated with the use of 1.5% glycine irrigation fluid resulting in the serious and occasionally fatal consequences discussed above.

However, there are now second generation ablative techniques which do not require the use of electrocautery or the use of glycine or other distension fluids. They avoid the serious risk of hyponatraemia and represent simpler, quicker and potentially more efficient means of treating menorrhagia.

A Cochrane Collaboration review (2013)[15] concludes that "*Overall, the existing evidence suggests that success, satisfaction rates and complication profiles of newer techniques of ablation compare favourably with hysteroscopic techniques.*"

NICE[16] in their online guidance for Heavy Menstrual Bleeding recommend,

- First-generation ablation techniques (e.g. rollerball endometrial ablation [REA] and TCRE) are appropriate if hysteroscopic myomectomy (TCRF) is to be included in the procedure.

- All women considering endometrial ablation should have access to a second-generation ablation technique.

Recommendation 3
Engineer changes in the type of procedures performed. • More secondary procedures for management of heavy menstrual bleeding as per NICE recommendations.

If hysteroscopic procedures such as TCRE and TCRF are considered to be the best options and a distending fluid is required, the choice of fluid then comes under the same scrutiny as above for Urology. The choice of using a monopolar scope system using glycine versus bipolar equipment using saline becomes the choice. Evidence is now emerging from gynaecology units in Northern Ireland that are measuring the serum sodium intraoperatively during every case, that there can be concerning incidences of acute hyponatraemia when glycine is used as the distending agent during TCRE[17]. With the development of newer bipolar systems it is recommended that saline has a better safety profile[3].

Therefore, this policy recommends that, (as long as they are proven to be safe and effective as judged by the NICE interventional procedure programme,) the use of second generation ablative techniques and bipolar RF systems should be introduced regionally and the use of glycine as a irrigant curtailed, strictly monitored when it is still used and eventually terminated when there ceases to be circumstances when its use is considered the safest.

4.2.3 Identification, control and management of haemorrhage.

Blood loss can be difficult to quantify and may be significant. Close attention to the patient's clinical state and good communication between surgeon, anaesthetist and the theatre team is vital.

Because of the generalised physiological effects of haemorrhage and the increased likelihood of fluid absorption when using irrigation fluid in the presence of 'open' vasculature, the presence of significant bleeding should act as a trigger for,

- increased vigilance for development of fluid overload, hyponatraemia.
- additional help from medical and nursing staff to assist by scrubbing in.
- increased frequency of haemoglobin and/or haematocrit measurements.
- preparation of blood for cross matching.
- control of the bleeding which may need cessation of the operation.

Recommendation 4
Increase vigilance when significant haemorrhage is a feature.

4.2.4 Control of the absorption of irrigation fluid

To control the effects of fluid absorption, the theatre team should pay particular attention to,

a) hyponatraemia.
b) limiting the volume of fluid absorbed.

a. Hyponatraemia

The uptake of 1000 ml of fluid would generally correspond to an acute decrease in the serum sodium concentration of 5-8 mmol/L.[2] Encephalopathy, seizures and even cerebral oedema may develop when the sodium concentration falls below 120mmol.L^{-1}. However, even markedly hyponatraemia patients may show no signs of water intoxication. The crucial physiological derangement of CNS function is not just hyponatraemia *per se*, but also the presence of acute hypo-osmolality[4].

Also, a patient's serum sodium concentration and osmolality may continue to decrease for some time after the procedure because irrigant can be slowly absorbed from the perivesicular and retroperitoneal spaces. Therefore, the TUR syndrome can start 4 to 24 hours later – postoperatively, in the recovery ward or back in the ward.

Whereas hyponatraemia occurs with equal frequency in men and women, premenopausal women are 25 times more likely to die or have permanent brain damage than men or postmenopausal women, most likely an oestrogen effect[3]. This effect is compounded because fluid absorption is slightly more common during TCRE than during TURP, and especially so with TCFR.

Serum Sodium measurement

Monitoring serum sodium concentration during TURP is common practice and a low value will confirm the diagnosis of hyponatraemia and is effective for assessing intravascular absorption. Significant decreases from a normal preoperative level can occur after just 15 minutes of starting resection. Levels below 120mmol.L^{-1} are invariably symptomatic and a rapid fall is more likely to produce symptoms.

Point-of-care testing (POCT) is defined as medical testing at or near the site of patient care. It brings the test conveniently and immediately to the patient increasing the likelihood that the patient, physician, and care team will receive the results in minutes, enabling diagnosis of hyponatraemia as early as possible and allowing immediate clinical management decisions to be made. They can be used to measure haematocrit, determine haemoglobin and measure serum electrolytes.

Serum sodium is often only measured at the end of surgery but, in the surgical settings pertaining herein, this monitoring technique is best applied before and repeatedly during surgery so that it can act as a warning system for hyponatraemia. Trusts already operating this method of monitoring have uncovered episodes of unsuspected hyponatraemia; highlighting the need to be wary of glycine and to monitor accordingly. Previous audits that have not

measured serum sodium as part of their audit criteria are thus likely to have given a false sense of security when using glycine.

Any patient receiving glycine in theatre **must** have such POCT equipment readily available and a measurement(s) made,

- as a preoperative baseline prior to the start of surgery.
- if the surgery is longer than 30 minutes.
- intermittently throughout a case as a routine.
- if there is a 1000 ml fluid deficit.

Staff must be readily available who are trained to use this POCT equipment and indeed immediately available to transport the samples and result to and from the machine.

NOTE: Measurement of serum sodium is not required when using a bipolar technique and saline[8].

Recommendation 5
If continue to use glycine, the following **MUST** be used, • Measure POCT serum sodium, i. preoperatively. ii. if the surgery is longer than 30 minutes. iii. intermittently throughout the surgery as a routine. iv. if there is a 1000 ml fluid deficit. • Dedicated staff for transporting specimens and results. • Surgery, including TURP, TCRE & TCRF must be performed in a 'main' theatre where POCT equipment is immediately available.

b. <u>Limit the volume of fluid absorbed.</u>
The choice of surgical technique and equipment may reduce the complications from irrigation fluid by limiting the use of glycine but continued attention to controlling fluid absorption will still be needed if normal saline is used as the distending fluid.

Basic principles govern the amount of fluid absorbed[18].

i. The hydrostatic driving pressure of the distending fluid. This is often a feature of the height of the container but the pressure may be controlled mechanically.
ii. Measurement, monitoring and documentation of the fluid volumes and deficits.
iii. The length of the surgical procedure.

i. Hydrostatic driving pressure of the distending fluid
Surgeons have a vital role in minimising absorption by keeping the cavity distention pressure at the lowest pressure necessary to distend, consistent with good visualisation. Even though the disruption in the vascular system is venous, the best strategy is to measure arterial pressures (which is easy to

do) and to maintain distending pressure below the mean arterial pressure (MAP).

It is estimated that approximately 40mmHg distending pressure is required to obtain clear vision. At pressures between 40mmHg and approximately 100mmHg (MAP), blood will continue to escape from disrupted capillaries until it is stopped by the tamponade. At this point, when continuous flow is used through the resectoscope, the blood within the cavity will be removed and a clear field of vision will be maintained. Dropping the pressure permits further bleeding. If the pressure is raised above the MAP, the pressure not only prevents the flow of blood out of disrupted vessels but actually forces the distension fluid medium in the reverse direction into the vessels.

There exist a number of fluid delivery systems, ranging from those based on simple gravity to automated pumps that are designed to maintain a pre-set intra-cavity pressure. Methods of instilling the distention fluid include,

- continuous-flow by gravity,
- continuous-flow infusion pump,
- pressure-controlled or pressure-sensitive fluid pumps.

Continuous-flow by gravity

In continuous-flow gravity systems, pressure is controlled by the height of the fluid source above the bladder or uterus and is measured from the height of the highest portion of the continuous column of fluid (fluid bag) to the level of the uterus or bladder – approximately 30 cms height is equivalent to 25 mm Hg pressure[19]. If the bag is 60 cms above the patient's uterus, this results in approximately 50 mm Hg of pressure.

Height of fluid column	Pressure exerted
12 inches ≡ 30 cms	25 mmHg
24 inches ≡ 60 cms	50 mmHg
36 inches ≡ 90 cms	75 mmHg

Gravity based systems are very simple to assemble and operate, but require vigilant patient monitoring and frequent manual intake/output calculations, which can be imprecise.

Recommendation 6
Limiting the distension pressure by, • maintaining it below the mean arterial pressure (MAP). • attempting to limit the height of the irrigating solution container to 60 cm above the patient and certainly never above 100cm. • Theatre teams must have a procedure for checking and maintaining an agreed height. • not applying pressure bags to the irrigation fluid bag.

Continuous-flow infusion pump

Continuous-flow fluid infusion pumps provide a constant flow of distention fluid at the in-flow pressure determined by the operator, delivering the same flow rate regardless of the out-flow conditions. Continuous flow pumps do not

usually monitor or calculate the intracavity pressure. Significant fluid absorption and complications can occur with these types of systems because the team is unaware of the actual pressure being used during a prolonged or invasive procedure.

Pressure-controlled or pressure-sensitive fluid pumps
Pressure-controlled infusion pumps can be preset to maintain a desired in-flow pressure. By adjusting the in-flow pressure setting on the pump, it can be maintained below the MAP, thus reducing the likelihood of intravasation.

These pumps can weigh the fluid volume before infusion, which allows them to account for the overfill often found in fluid bags. Weight of fluid before installation and then after, accounts for the deficit, which provides a more accurate measurement of the fluid retained by the patient (fluid deficit). A continuous automated weighing system provides an easy, less time-consuming and valid method of monitoring fluid deficit[2] and an automated fluid management system is recommended[3].

Recommendation 7
Investigate instilling irrigation fluid by using a pressure controlled pump device and purchasing flow/pressure controllers.

ii. Measurement, monitoring and documentation of the fluid volumes & deficits.
If continuous irrigation using fluid filled bags and gravity continue to be used, volumetric fluid balance is based on counting the number of empty fluid bags and then subtracting the out-flow volume in the collection canister and fluid in the drapes to determine irrigation fluid deficit. Positive values are regarded as absorption. The surgeon should be notified about ongoing fluid absorption early enough for steps to be taken to prevent excessive absorption.

However[1], calculation of systemic absorption is complicated by 4 factors:
1. It may be difficult to collect all of the media (fluid, urine and blood) that passes out of the operative area, including that which falls on the procedure or operating room floor.
2. the actual volume of media solution in 3L bags is typically more than the labelled volume.
3. difficulties in estimating the volume of media left in a used or ‘emptied’ infusion bag.
4. systemic absorption that in some instances may occur extremely rapidly.

While these factors can make volumetric fluid balance measurement an unreliable tool, it is considered a minimum necessity when using fluid filled bag systems that the whole theatre team are aware of the distending fluid input & output and the irrigation fluid deficit. This is especially true for cases where glycine is used.

A member of staff must be assigned to this duty before the start of every case. They will need to be proficient and practiced in this technique and must take

responsibility for measuring the input and output, calculating the deficit and recording these details. They should remain in theatre for the duration of the procedure, in the same fashion as the surgeon.

Recommendation 8
The theatre team **must**, • be aware of the distending fluid input & output and deficit. • contain a dedicated nurse for fluid balance and deficit calculation, who remains in theatre for the duration of the procedure.

When using a pressure-controlled infusion pump to control the distension fluid with their associated continuous automated weighing system, the monitoring of the fluid deficit is easier[2], less time-consuming and thus an automated fluid management system is recommended[3].

Documentation

Each patient who has any irrigating fluid used must have documentation in the way of a dedicated fluid management chart (appendix 1) commenced. This can be either the measurement of input & outputs and calculating the deficit or recording the readings off an automated machine.

This should be done as a minimum every time a bag (often 3 litre) is hung up and the details clearly expressed verbally to the surgeon and all other theatre staff. These details should be recorded on the dedicated fluid management chart. They might also be displayed on a white marker board in the theatre.

At the end of the procedure, the final calculations or readings must be made; the inputs, outputs and deficit. These should be expressed clearly to the surgeon and anaesthetist and recorded on the chart. The operating surgeon should include the fluid deficit in the *Operative Findings* when writing the operative notes.

The fluid management chart must follow the patient into the recovery ward. All fluid balances must be handed over to recovery ward staff as part of the normal nursing and medical handover. The chart is then to be filed in the clinical record.

Recommendation 9
If continue to use glycine, the following **MUST** be used, throughout the procedure, • Accurate irrigation fluid input & output measurement and deficit calculation.

Maximum fluid deficit

Prevention of the TUR syndrome requires that the team have a protocol for responding to any escalating fluid absorption and there must be agreed

volume thresholds for action. These thresholds may necessarily vary depending on the,

- nature of the surgery,
- nature of the media (isotonic or hypotonic) ,
- patient's baseline,
- intraoperative medical condition e.g. presence of haemorrhage.

Considering glycine use, a 500 ml threshold may be appropriate for those who are older and/or medically compromised while for healthy individuals absorption of up to 1000 mL can generally be tolerated. Greater than 1000 mL of glycine intravasation results in a significant decrease in serum sodium, sufficient to bring a normo-natraemic patient into the abnormal range[1, 2, 3].

The surgeon and anaesthetist must be informed by the nurse when there is a 1000mls glycine deficit. Surgery must be brought to a close unless continuation of surgery is absolutely necessary to control the haemorrhage. The nurse must ensure that the surgeon and anaesthetist acknowledge that they have received this information. This must be documented in the notes along with any action taken.

Considering normal saline use, the maximum limit is unclear, but 2500 mL has been advocated[3]. Surgery must be brought to a close unless haemorrhage needs controlled.

Recommendation 10
Preoperatively, there **must** be an agreed maximum fluid deficit threshold for action. The surgeon and anaesthetist **must** be informed by the nurse when the threshold is reached.

iii. The length of the surgical procedure.
Estimates of the amount of fluid absorbed range from 10 – 30 mls per minute of resection time; over a 45 – 60 minute case that could equate to 1 – 1.8 litres.

Operation time; procedures that last longer than 60 minutes and those that require large amounts of tissue resection are more likely to lead to fluid volume overload. Theatre teams must have an established mechanism for measuring time and procedures for alerting surgeon and anaesthetist.

Recommendation 11
Operations should not last longer than 60 minutes. Theatre teams **must** have an established mechanism for measuring time and procedures for alerting surgeon and anaesthetist.

4.2.5 Theatre environment

A good theatre environment in terms of team dynamics is essential for the safe performance of these surgical procedures. There must be careful monitoring of fluid balance along with the clear communication of that balance to the surgical and anaesthetic members of the team.

- Theatre staff must always be aware of the potential hazards of, and equipment used, for any surgical procedure before it is performed.
- One core member of the theatre team must be assigned to the duty of gathering together the information needed to ensure the whole theatre team are aware of the distending fluid input & output and the deficit. They will need to be proficient and practiced in this technique and must not have other duties to perform while monitoring fluid balance. It would not be expected that the surgeon should have to operate and also supervise this function at the same time. They should remain in theatre for the duration of the procedure, in the same fashion as the surgeon.
- Medical staff must always have situational knowledge of the theatre environment that they are working in and the availability (or non-availability) of any theatre equipment they consider necessary. They must be informed, in good time, of any equipment that is not working.
- Nursing staff should have a working knowledge of any equipment being used in their theatre or have the immediate presence of technical staff who do have that knowledge.

4.2.6 WHO checklist

Completion of the WHO surgical checklist with the sign in, time out and sign out must be adhered to. This will allow a surgical, anaesthetic and theatre team brief at the beginning for the whole theatre team and an opportunity to check that everything is in place to perform the biochemical and volumetric monitoring, to agree fluid absorption volume limits and should include any discussion of limiting intravenous fluids intraoperatively.

It will also ensure at the sign out that any problems e.g. over a fluid deficit, are identified early. On a regional basis, adoption of a modified WHO checklist for this kind of procedure should be investigated and piloted.

Recommendation 12
Completion of the WHO surgical checklist **must** be adhered to. Adoption of a modified WHO checklist for this kind of procedure should be investigated and piloted.

5.0 IMPLEMENTATION OF POLICY

This policy, after it is agreed, is to be implemented throughout NI in each of the 5 Trusts.

5.1 Resources

There will be resource implications in terms providing surgical equipment that can be used without needing glycine as an irrigant, fluid flow and pressure controllers and POCT monitoring equipment for theatres and training for staff.

6.0 MONITORING

Trust audit departments will need to monitor that the recommendations are implemented.

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8.0 CONSULTATION PROCESS

Consulted through the Medical Leaders Forum, DHSSPSNI, and via the Medical Directors, Directors of Nursing and Regional Urologists, Gynaecologists and Anaesthetists.

9.0 APPENDICES / ATTACHMENTS

Appendix 1 = Suggested peri-operative theatre record form template.

10.0 EQUALITY STATEMENT

In line with duties under the equality legislation (Section 75 of the Northern Ireland Act 1998), Targeting Social Need Initiative, Disability discrimination and the Human Rights Act 1998, an initial screening exercise to ascertain if this policy should be subject to a full impact assessment has been carried out. The outcome of the Equality screening for this policy is:

Major impact ☐

Minor impact ☐

No impact. ☐

SIGNATORIES

_____ **Date:** _____

Author

_____ **Date:** _____

Author

_____ **Date:** _____

Director

Trust LOGO

Peri-operative fluid recording chart

Date: _____

Surgeon: _____

Anaesthetist: _____

Team Leader: _____

Circulating Nurse 1: _____

Circulating Nurse 2: _____

Addressograph Label

Fluid recorder: _____ Operation: _____

Fluid Medium: 3L 1.5% Glycine: ☐ 0.9% NaCl: ☐ Warmed: ☐

Bag Height: _____ mmHg ☐ (60 cms ≡ 50mmhg)

Preop. Serum Sodium: = _____ mmol/L Haemoglobin: _____ g/dL.

Resection: Start Time: _____:_____ Operation Finish Time: _____:_____

Irrigation fluid: Start time: _____:_____ **= 0 mins.**

Time (min)	Irrigation In	Irrigation Out	Irrigation Deficit	Running Deficit	Serum Sodium	Surg. informed	Anaes. informed	Sign
5	mls	mls	mls	mls	mmol/L			
10	mls	mls	mls	mls	mmol/L			
15	mls	mls	mls	mls	mmol/L			
20	mls	mls	mls	mls	mmol/L			
25	mls	mls	mls	mls	mmol/L			
30	mls	mls	mls	mls	mmol/L			
35	mls	mls	mls	mls	mmol/L			
40	mls	mls	mls	mls	mmol/L			
45	mls	mls	mls	mls	mmol/L			
50	mls	mls	mls	mls	mmol/L			
55	mls	mls	mls	mls	mmol/L			
60	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			

Total Fluid In =	mls	Surgeon Signature	
Total Fluid Out =	mls	Anaesthetist Signature	
Total Deficit =	mls	Nurse Signature	
		Recovery Staff Signature	

Trust LOGO

Continued.

Time (mins)	Irrigation In	Irrigation Out	Deficit	Running deficit	Serum Sodium	Surg. informed	Anaes. informed	Sign
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			
	mls	mls	mls	mls	mmol/L			

Irrigation In	Document number of mls after each fluid bag is emptied. Record amount 'in' each time use Ellick evacuator.
Irrigation Out	Record fluid in • suction canisters. • fluid in drapes. • fluid from floor suction. Record amount 'out' each time use Ellick evacuator.
Deficit	Calculate deficit or record from pump readout.
Serum Sodium	Ensure there is a Serum Sodium measurement within one bold bordered box if procedure longer than 30 mins.

Glycine		
Volume Absorbed	**Effect**	**Action**
500 mls	Limit for the Elderly : comorbidities	Continue surgery
less than 1000 mls	Well tolerated by healthy patient	Continue Surgery
greater than 1000 mls	Mild hyponatraemia	Complete surgery ASAP
1500 mls	**Severe hyponatraemia & other biochemical disturbances likely**	**Stop Surgery**
Normal Saline		
2000 mls	Limit in the healthy	Complete surgery ASAP

NICE National Institute for Health and Care Excellence

The TURis system for transurethral resection of the prostate

Issued: February 2015

NICE medical technology guidance 23

guidance.nice.org.uk/mtg23

NICE has accredited the process used by the Centre for Health Technology Evaluation at NICE to produce medical technologies guidance. Accreditation is valid for 5 years from November 2011 and applies to guidance produced since March 2011 using the processes described in NICE's 'Medical Technologies Evaluation Programme: methods guide' (2011) and 'Medical Technologies Evaluation Programme: process guide' (2011). More information on accreditation can be viewed at www.nice.org.uk/accreditation

NICE accredited
www.nice.org.uk/accreditation

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1 Recommendations

NICE medical technologies guidance addresses specific technologies notified to NICE by companies. The 'case for adoption' is based on the claimed advantages of introducing the specific technology compared with current management of the condition. This case is reviewed against the evidence submitted and expert advice. If the case for adopting the technology is supported, then the technology has been found to offer advantages to patients and the NHS. The specific recommendations on individual technologies are not intended to limit use of other relevant technologies which may offer similar advantages.

1.1 The case for adopting the transurethral resection in saline (TURis) system for resection of the prostate is supported by the evidence. Using bipolar diathermy with TURis instead of a monopolar system avoids the risk of transurethral resection syndrome and reduces the need for blood transfusion. It may also reduce the length of hospital stay and hospital readmissions.

1.2 Using the transurethral resection in saline (TURis) system instead of monopolar transurethral resection of the prostate (TURP) results in an estimated saving of £71 per patient for hospitals that already use an Olympus monopolar system and an estimated additional cost of £20 per patient for other hospitals. However, there is some evidence of a reduction in readmissions with the TURis system compared with monopolar TURP. If this evidence is included, using the TURis system results in an estimated saving of £375 per patient for hospitals that already use an Olympus monopolar system and an estimated saving of £285 per patient for other hospitals.

2 The technology

Description of the technology

2.1 Transurethral resection in saline (TURis, Olympus Medical) is a bipolar electrosurgery system designed for use when surgical intervention is indicated for prostatic enlargement.

2.2 The TURis system consists of an Olympus generator, a resectoscope, which incorporates the TURis active working element and electrode, a telescope, an inner and outer sheath, a light guide cable, and a saline cable. The active and return electrode are contained within the resectoscope at the site of the operation, eliminating the need for a patient return electrode because TURis uses saline irrigation fluid to conduct electrical current within the resectoscope. The surgeon uses an endoscopic image to guide the electrode assembly through the urethra to the prostate. The electrode is then used to cut and coagulate prostate tissue and saline is used to flush the bladder free of resected prostate tissue and blood. Electrodes are available in different sizes and shapes (described as loop, button and roller) for cutting or coagulation and to take into account surgeon choice. Generally a loop is used to repeatedly cut out small chippings to create a wide channel through the prostate and a roller or button may be used to achieve haemostasis. The prostatic chippings are flushed out before inserting a urethral urinary catheter at the end of the procedure.

2.3 The components of the TURis system are covered by individual CE marks. The most recent of these was issued in 2013 for the TURis working element.

2.4 The list prices for the components of the TURis system for transurethral resection of the prostate (excluding VAT) are:

- £8905 for the resectoscope assembly (which includes the active working element, telescope, inner and outer sheath, light guide cable and saline cable).
- £14,681 for an ESG-400 Olympus generator.

- Single-use roller and loop electrodes are £156.67 and £126.67 respectively. Each TURis procedure uses 1 loop electrode and some procedures, typically 1 in 5, use an additional roller electrode.

  The ESG-400 Olympus generator is usually provided at no cost as part of contractual arrangements with Olympus to purchase electrodes at list price.

2.5 The claimed benefits of the TURis system for transurethral resection of the prostate presented by the company were:

- Reduced risk of transurethral resection syndrome through the use of saline irrigation fluid.
- Reduced risk of postoperative blood transfusion because of intraoperative bleeding.
- A shorter length of stay in hospital due to a shorter surgical procedure and fewer intra- and postoperative complications.
- Earlier catheter removal time for improved patient comfort.
- A quicker procedure compared with monopolar transurethral resection of the prostate (TURP) so more men can be treated.
- Fewer complications during and after surgery resulting in lower readmission rates.
- Reduced costs (associated with postoperative blood transfusion, healthcare-associated infection, length of hospital stay, postoperative irrigation and a patient return electrode).
- The use of saline irrigation fluid is cheaper and more readily available than glycine.

Current management

2.6 The NICE guideline on lower urinary tract symptoms defines benign prostate enlargement as an increase in the size of the prostate gland because of benign prostatic hyperplasia, and states that about 50% of men with benign prostatic hyperplasia will develop benign prostatic enlargement. It recommends that surgery is offered only if voiding lower urinary tract symptoms are severe or if

drug treatment and conservative management options have been unsuccessful or are not appropriate.

2.7 For surgical treatment of benign prostatic enlargement, the NICE guideline on lower urinary tract symptoms recommends the use of monopolar or bipolar TURP, monopolar transurethral vaporisation of the prostate or holmium laser enucleation of the prostate.

2.8 The NICE guideline on lower urinary tract symptoms also recommends some alternative options:

- Transurethral incision of the prostate (TUIP) can be offered as an alternative to other types of surgery to men with a prostate estimated to be smaller than 30 g.
- Open prostatectomy should only be offered as an alternative to other types of surgery to men with prostates estimated to be larger than 80 g.
- Other alternatives such as laser vaporisation techniques, bipolar transurethral vaporisation of the prostate or monopolar or bipolar transurethral vaporisation resection of the prostate should only be considered as part of a randomised controlled trial that compares these techniques with TURP.

3 Clinical evidence

Summary of clinical evidence

3.1 The key clinical outcomes for the transurethral resection in saline (TURis) system for transurethral resection of the prostate presented in the decision problem were:

- hospital length of stay
- procedural blood loss and blood transfusion
- time to removal of urinary catheter postoperatively
- transurethral resection syndrome
- readmission for repeat procedures
- duration of surgical procedure
- healthcare-associated infection
- quality of life
- device-related adverse events.

3.2 The company identified a total of 1116 studies in their database searches, and presented 24 studies in their submission as relevant to the decision problem. These included 14 randomised trials, not all of which were published in full or in English, with a total of 3032 patients (Abascal Junquera et al. 2006; Akman et al. 2013; Chen et al. 2009, 2010; Fagerstrom et al. 2010, 2011; Goh et al. 2009, 2010; Gulur et al. 2010a, 2010b; Michielsen et al. 2007, 2010a, 2010b; Rose et al. 2007) and 10 observational studies (Bertolotto et al. 2009; Fumado et al. 2011; Giulianelli et al. 2012; Ho et al. 2007; Jun Hyun et al. 2012; Lee et al. 2011; Michielsen et al. 2010c, 2011; Petkov et al. 2011; Puppo et al. 2009).

3.3 The External Assessment Centre considered the 14 randomised trials described in the submission. It established that the 3 randomised studies and

2 observational studies published by Michielsen reported on various stages and subgroups of the same study population. It also considered that the 2 papers from Fagerstrom were based on the same study population, and that the 4 conference abstracts (Goh et al. 2009, 2010; Gulur et al. 2010a, 2010b) were based on the same study population. Two studies were not published in English but have English abstracts (Abascal Junquera et al. 2006; Rose et al. 2007). The External Assessment Centre considered that, of these, only the Rose et al. (2007) paper contained pivotal results and it obtained a translation of the paper; the other was not considered pivotal. A literature search by the External Assessment Centre identified 2 further randomised studies (Geavlete et al. 2011; Ho et al. 2006). In total the External Assessment Centre considered that there were 10 unique randomised studies (1870 patients) relevant to the decision problem, 9 published as papers (including 2 foreign language papers with English abstracts) and 1 abstract.

3.4 The company presented 10 observational studies, 5 of which were published in full and 5 of which were abstracts only. The External Assessment Centre established that the Michielsen et al. (2010 and 2011) studies reported on subgroups from the randomised study by Michielsen et al. published in 2007. A literature search by the External Assessment Centre identified 1 additional observational study (Shum et al. 2014). The External Assessment Centre considered that there were 4 published papers and 5 abstracts describing relevant observational studies. It agreed with the company's conclusion that the outcomes reported from the observational studies were consistent with those from the randomised trials. The observational studies are summarised in the assessment report and are not considered further here.

Randomised trials: published papers

3.5 Akman et al. (2013) reported a Turkish study of 286 men (143 in each group) randomised to have either TURis or monopolar transurethral resection of the prostate (TURP) who were followed-up for 12 months. The mean procedure duration was 54.0 minutes for TURis and 58.7 minutes for monopolar TURP, p=0.03. The incidence of TUR syndrome was 0% for TURis and 1.5% for monopolar TURP (no p value reported). There was no statistically significant difference in the length of hospital stay for the TURis group compared with the monopolar TURP group (2.5 days compared with 2.7 days, no p value

reported). The rate of blood transfusion was lower in the TURis group (2.4% compared with 6.2%) but the difference was not statistically significant (p=0.2). There were lower rates of clot retention (0.8% compared with 1.5%, p value not reported) and mean time to catheter removal (2.4 days compared with 2.6 days, p value not reported) for TURis.

3.6 The Chen et al. (2009) study was done in China on 45 men with symptomatic benign prostatic hypertrophy and a large prostate gland, randomised to have either TURis or monopolar TURP. Results were analysed for 40 men, with reasons given for withdrawals. The results showed that average procedure duration was shorter in the TURis group compared with the monopolar TURP group (88 minutes compared with 105 minutes, p=0.001). No men in the TURis group had TUR syndrome, compared with a 5% rate (n=1/19) in the monopolar TURP group. Fewer men had a blood transfusion in the TURis group (4.8% compared with 15.5%, p value not reported). There was no statistically significant difference between groups in the time to catheter removal (2.5 days compared with 3.4 days, p=0.11). However there was a statistically significant reduction in length of hospital stay for the TURis group (3 days compared with 4.2 days, p=0.001).

3.7 Chen et al. (2010) reported a separate study of 100 men in China randomised to have either TURis or monopolar TURP. There was no statistically significant difference in procedure duration in the TURis group compared with the monopolar TURP group (59 minutes compared with 60 minutes, p=0.82) or weight of tissue resected (40 g compared with 38.9 g, p=0.31). No patient in either group had TUR syndrome. One man in the TURis group and 3 men in the monopolar TURP group needed a blood transfusion (2% compared with 6%, p=0.62).

3.8 The Fagerstrom et al. (2009 and 2011) studies were performed in Sweden on 202 men randomised to have either TURis or monopolar TURP. Results were analysed for 185 men, with reasons given for withdrawals. Results showed that there was no statistically significant difference between the TURis and monopolar TURP group in mean procedure time (62 minutes compared with 66 minutes, p not significant) or weight of tissue resected (27.3 g compared with 26.3 g, p not significant). No patient developed TUR syndrome in the

TURis group, but 3 did so in the monopolar TURP group. A statistically significantly lower proportion of men in the TURis group had a blood transfusion (4% compared with 11%, p<0.01). Median time to catheter removal was the same in both groups (20 hours), and the length of stay in hospital was similar (51 hours compared with 52 hours). There was a statistically significant reduction in the rate of readmission in the TURis group (n=5/98 compared with n=14/87, p<0.011).

3.9 The Geavlete et al. (2011) study involved 510 men in Romania who were randomised to 3 study arms (170 in each arm). Results are reported here for the TURis and monopolar TURP arms (340 patients), but not for the bipolar plasma vaporisation of the prostate arm which was considered to be outside the scope. Statistical analysis was performed on the difference between the 3 groups and is not reported here. The average procedure duration was 52.1 minutes in the TURis group and 55.6 minutes in the monopolar TURP group. No men had TUR syndrome in the TURis group compared with 3 men (1.8%) in the monopolar TURP group. In the TURis group 3 men (1.8%) needed a blood transfusion, compared with 11 men (6.5%) in the monopolar TURP group. In the TURis group 2 men (1.2%) had clot retention compared with 7 men (4.1%) in the monopolar TURP group. The mean time to catheter removal was 46.3 hours (range 36–72 hours) in the TURis group compared with 72.8 hours (range 48–96 hours) in the monopolar TURP group. In the TURis group length of stay in hospital was 3.1 days compared with 4.2 days in the monopolar TURP group.

3.10 The Ho et al. (2007) study was performed in Singapore on 48 men randomised to TURis and 52 men randomised to monopolar TURP. There was no statistically significant difference in mean procedure duration between the groups (59 minutes for TURis compared with 58 minutes for monopolar TURP) or in the weight of tissue resected (29.8 g TURis compared with 30.6 g monopolar TURP). There was a statistically significantly lower rate of TUR syndrome in the TURis group compared with the monopolar TURP group (0 men compared with 2 men, p<0.005). One patient in each group needed a blood transfusion. In the TURis group 3 men had clot retention compared with 2 men in the monopolar TURP group; this difference was not statistically significant.

3.11 The Michielsen et al. (2007) study recruited patients between January 2005 and June 2006 in Belgium. However, recruitment into the study continued until August 2009, leading to subsequent papers reported as randomised (Michielsen et al. 2010a, 2010b) and observational studies (Michielsen et al. 2010c, 2011). In total 550 patients were included in the study; 285 in the TURis group and 265 in the monopolar TURP group, but some outcomes were reported on smaller groups. There was no significant difference between the TURis group (n=263) and monopolar TURP group (n=255) in mean procedure duration (52.1 minutes compared with 50.9 minutes, p=0.357) or mean weight of tissue resected (17.6 g compared with 19.2 g, p=0.173). TUR syndrome did not occur in the TURis group and occurred twice (0.8%) in the monopolar TURP group (p value not reported). In the TURis group (n=118) 4 men (3.4%) needed a blood transfusion compared with 1 patient (0.8%) in the monopolar TURP group (n=120, p=0.211). There was no statistically significant difference in mean length of hospital stay: 3.72 days in the TURis group (n=263) and 3.89 days in the monopolar TURP group (n=255, p=0.773). No patients in the TURis group (n=118) and 2 patients in the monopolar TURP group (n=120) needed a repeat procedure because of incomplete resection (p value not reported).

3.12 The Rose et al. (2007) study was published in German and the External Assessment Centre obtained an English translation. It included 38 men who had TURis and 34 men who had monopolar TURP (the remainder had treatment for bladder cancer) in Germany. Mean procedure duration was longer in the TURis group than in the monopolar TURP group (55 minutes compared with 35 minutes, p=0.005), but the mean weight of tissue resected tended to be greater in the TURis group (42 g compared with 31 g, p value not reported). No men had TUR syndrome in either group. The mean time to catheter removal was longer in the TURis group (64 hours compared with 49 hours, p value not reported) and the TURis group had a higher rate of readmission because of haemorrhage (n=4/38 compared with n=1/34, p value not reported).

3.13 The Abascal Junquera et al. (2006) study was published in Spanish with an English abstract that had limited information on the statistical analysis. The External Assessment Centre considered that the study did not provide