

Appendix A: Summary of evidence from surveillance

2019 surveillance of Lower urinary tract symptoms in men: management (2010) NICE guideline CG97

Summary of evidence from surveillance

Studies identified in searches are summarised from the information presented in their abstracts.

Feedback from topic experts who advised us on the approach to this surveillance review, was considered alongside the evidence to reach a view on the need to update each section of the guideline.

Evidence from an Evidence Update for this topic was also considered. Evidence updates were produced by NICE to highlight new evidence relating to published NICE guidelines.

1.1 Initial assessment

Recommendations in this section of the guideline

- 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.
- 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 (DRE).
- 1.1.3 At initial assessment, ask men with bothersome LUTS to complete a urinary frequency volume chart.
- 1.1.4 At initial assessment, offer men with LUTS a urine dipstick test to detect blood, glucose, protein, leucocytes and nitrites.
- 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 BPE or
 - their prostate feels abnormal on DRE or
 - they are concerned about prostate cancer.
- 1.1.6 Manage suspected prostate cancer in men with LUTS in line with the NICE guidelines on prostate cancer and referral guidelines for suspected cancer.
- 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).
- 1.1.8 Do not routinely offer cystoscopy to men with uncomplicated LUTS (that is, without evidence of bladder abnormality) at initial assessment.
- 1.1.9 Do not routinely offer imaging of the upper urinary tract to men with uncomplicated LUTS at initial assessment.
- 1.1.10 Do not routinely offer flow-rate measurement to men with LUTS at initial assessment.
- 1.1.11 Do not routinely offer a post void residual volume measurement to men with LUTS at initial assessment.
- 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.
- 1.1.13 Offer men referral for specialist assessment if they have bothersome LUTS that have not responded to conservative management or drug treatment.
- 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.
- 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.

Surveillance proposal

These recommendations should not be updated.

Initial assessment

Flow-rate measurement

Previous surveillance summary

No new evidence was identified during the 2012 Evidence update. Evidence from an observational study (1) in 60 men with lower urinary tract symptoms (LUTS) identified during the 2014 surveillance review, supported application of a home-based digital urinary flow measuring device.

2019 surveillance summary

No relevant evidence was identified.

Intelligence gathering

No relevant information was identified.

Impact statement

The 2014 review found evidence that supported application of a home-based digital urinary flow measuring device. There is insufficient new evidence to enable a recommendation to be made on home-based digital urinary flow measuring device.

Current recommendation states: Do not routinely offer flow-rate measurement to men with LUTS at initial assessment (1.1.10)

New evidence is unlikely to change guideline recommendations.

1.2 Specialist assessment

Recommendations in this section of the guideline

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.
- 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 (DRE).
- 1.2.3 At specialist assessment, ask men with LUTS to complete a urinary frequency volume chart.
- 1.2.4 At specialist 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 BPE or
 - their prostate feels abnormal on DRE or
 - they are concerned about prostate cancer.
- 1.2.5 Offer men with LUTS who are having specialist assessment a measurement of flow rate and post void residual volume.
- 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.
- 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.
- 1.2.8 Consider offering multichannel cystometry to men with LUTS having specialist assessment if they are considering surgery.
- 1.2.9 Offer pad tests to men with LUTS having specialist assessment only if the degree of urinary incontinence needs to be measured.

Surveillance proposal

These recommendations should not be updated.

Specialist assessment

Cystoscopy

Previous surveillance summary

No new evidence was identified during the 2012 Evidence update. In the 2014 review, one study (2) found cystoscopy accurately distinguished patients with haematuria who were likely to have or not have bladder cancer.

2019 surveillance summary

No relevant evidence was identified.

Ultrasound

Previous surveillance summary

No new evidence was identified in the 2012 Evidence update. Findings from 2 studies (3,4) identified in the 2014 review indicated that ultrasound had high sensitivity and specificity for diagnosing infravesical obstruction (IVO) and enabled non-invasive assessment of LUTS.

2019 surveillance summary

No relevant evidence was identified.

Urinary flow rate and urodynamic testing

Previous surveillance summary

No new evidence was identified in the 2012 Evidence update. The 2014 review identified 1 study (1) in men with LUTS which investigated the accuracy of uroflowmetry with disposable Q(Single) compared with a home-based digital device or with a clinic-based method. Mean Q max obtained with Q(Single) device did not differ from that obtained with the clinic method.

2019 surveillance summary

Qualitative review from an RCT (5) assessed the experiences of urodynamic testing among 41 men aged 52-89 with LUTS. The 25 men who had experienced urodynamics all found it acceptable, though some reported pain, infection, or embarrassment.

A Cochrane systematic review (6) of 2 RCTs assessed whether invasive urodynamic investigation compared with non-invasive methods of diagnosis such as non-invasive urodynamics or clinical history and examination alone, reduces the number of men with symptoms of voiding dysfunction. There was insufficient information from the trials to demonstrate any reduction in s voiding dysfunction.

Intelligence gathering

Topic experts highlighted the following:

- One topic expert stated that flow chart for care pathway at initial assessment could be more specific: IPSS (International Prostate Symptom Score) assessment and PSA (Prostate specific

antigen) test should be considered at the initial assessment stage.

Impact statement

Cystoscopy

One study noted that cystoscopy accurately identified patients with haematuria who were likely to have or not have bladder cancer. As cystoscopy is currently recommended in men with LUTS if they have a history of haematuria, this new evidence is unlikely to change the recommendations.

Ultrasound

New evidence demonstrated that ultrasound had high sensitivity and specificity for diagnosing infravesical obstruction (IVO) and suprapubic transabdominal ultrasonographic enabled non-invasive assessment of LUTS.

Currently imaging of the upper urinary tract is only recommended for men with LUTS having specialist assessment and only when clinically indicated. No specific imaging modality is recommended; therefore, this new evidence is unlikely to impact on the guideline recommendation.

Urinary flow rate and urodynamic testing

New evidence is limited and does not support the use of invasive urodynamic investigation in men with LUTS.

One topic expert commented that PSA (Prostate specific antigen) test should be considered at the initial assessment stage of the care pathway however, no new evidence was found to support this.

New evidence is unlikely to change guideline recommendations.

1.3 Conservative management

Recommendations in this section of the guideline

- 1.3.1 Explain to men with post micturition dribble how to perform urethral milking.
- 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.
- 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.
- 1.3.4 Offer men with storage LUTS suggestive of overactive bladder (OAB) supervised bladder training, advice on fluid intake, lifestyle advice and, if needed, containment products.
- 1.3.5 Inform men with LUTS and proven bladder outlet obstruction that bladder training is less effective than surgery.

- 1.3.6 Offer supervised pelvic floor muscle training to men with stress urinary incontinence caused by prostatectomy. Advise them to continue the exercise for at least 3 months before considering other options.
- 1.3.7 Refer for specialist assessment men with stress urinary incontinence.
- 1.3.8 Do not offer penile clamps to men with storage LUTS (particularly urinary incontinence).
- 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 1.3.11).
- 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.
- 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.
- 1.3.12 If offering long-term indwelling catheterisation, discuss the practicalities, benefits and risks with the man and, if appropriate, his carer.
- 1.3.13 Explain to men that indwelling catheters for urgency incontinence may not result in continence or the relief of recurrent infections.
- 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.

Surveillance proposal

These recommendations should not be updated.

Conservative management

Sheaths

Previous surveillance summary

The 2012 Evidence update included a crossover RCT ([Chartier-Kastler et al. 2010](#)) that showed one particular sheath device improves QoL compared with incontinence pads. The 2014 review identified an RCT (7) that compared Uri-sheaths with absorbent products in men with moderate to severe urinary incontinence and concluded that most patients preferred Uri-sheaths to their usual absorbent products.

2019 surveillance summary

No relevant evidence was identified.

Catheterisation

Previous surveillance summary

No new evidence was identified in the 2012 Evidence update. Two systematic reviews on catheterisation were identified in the 2014 review. One systematic review reported minor complications following catheterisation, including urine leakage (8). The second systematic review (9) indicated that a hydrogel coated latex catheter was better tolerated than a silicone catheter.

2019 surveillance summary

No relevant evidence was identified.

Medications compared with conservative therapies

Previous surveillance summary

No evidence was identified in the 2012 Evidence update. From the 2014 surveillance review 1 RCT (10) and 2

systematic reviews(11,12) that compared antimuscarinics with conservative treatments were identified. Overall findings showed that antimuscarinics had greater benefits compared with conservative treatment.

2019 surveillance summary

An RCT (13) compared multicomponent behavioural treatment and exercise therapy (M-BET) with an active drug comparator (tamsulosin, one 0.4 mg tablet nightly) used alone or in combination (M-BET plus alpha blocker) for improving nocturia in 72 men. At 12 weeks, reductions in nocturia reductions similar across treatment groups. However, M-BET showed significant improvements in sleep quality, and nocturia-specific quality of life.

Pelvic floor exercises

Previous surveillance summary

No new evidence was identified in the 2012 Evidence update. In the 2014 review, 5 RCTs (14–18) and 3 systematic reviews (19–21) had contradictory results about the benefits of pelvic floor muscle training for reducing urinary incontinence. The studies on pelvic floor muscle training were heterogeneous; conducted in different populations and utilised different protocols for treatment.

2019 surveillance summary

No relevant evidence was identified.

Training program to improve physical activity

previous surveillance summary

No new evidence was identified in the 2012 Evidence update. The 2014 review

identified one RCT (22) which found a training program among residents in nursing homes improved urinary incontinence.

2019 surveillance summary

No relevant evidence was identified.

Biofeedback versus any other conservative therapy

previous surveillance summary

No new evidence was identified at the 2012 Evidence update. The 2014 review identified an RCT (23) which found that preoperative biofeedback combined with an assisted low-intensity programme of postoperative perineal physiokinetic therapy was significantly better than a control in reducing the incidence, duration and severity of urinary incontinence in patients undergoing radical prostatectomy.

2019 surveillance summary

No relevant evidence was identified.

Intelligence gathering

No relevant information was identified.

Impact statement

Sheaths

The 2012 Evidence update found an RCT demonstrating that one sheath device has some QoL benefit over incontinence pads which supports the current recommendation that men with LUTS should be offered a choice of containment products based on individual circumstances.

Catheterisation

Evidence from a systematic review identified in 2014 review indicated that a hydrogel coated latex catheter rather than a silicone catheter may be better tolerated. The guideline does not currently specify a type of catheter and additional studies focusing on benefits, harms and patient reported outcomes would be necessary before a specific recommendation about catheter type could be made.

Medications compared to conservative therapies

Evidence from 2014 review was in favour of antimuscarinics compared with conservative management for LUTS treatment. The guideline recommends that men with LUTS should only be offered drug treatment when conservative therapy has failed or is not appropriate; this new evidence is insufficient to change this recommendation.

Pelvic floor exercises

Supervised pelvic floor muscle training is currently recommended for men with stress urinary incontinence caused by prostatectomy and evidence identified in the 2014 is contradictory. Thus, there is no consistent new evidence which would change this recommendation.

Training program to improve physical activity

Evidence from an RCT identified in 2014 review suggested benefits of training program designed to improve physical capacity among residents in nursing homes to improve urinary incontinence. However, additional evidence on the benefits and

harms in men with LUTS compared with other conservative therapies is needed before considering this intervention for inclusion in the guideline.

Biofeedback versus any other conservative therapy

The evidence from an RCT at 2014 review suggests that preoperative biofeedback combined with an assisted low-intensity programme reduces the incidence,

duration and severity of urinary incontinence in patients undergoing radical prostatectomy. The guideline has no recommendations on biofeedback and the new evidence is insufficient to enable a recommendation to be made.

New evidence is unlikely to change guideline recommendations.

1.4 Drug treatment

Recommendations in this section of the guideline

- 1.4.1 Offer drug treatment only to men with bothersome LUTS when conservative management options have been unsuccessful or are not appropriate.
- 1.4.2 Take into account comorbidities and current treatment when offering men drug treatment for LUTS.
- 1.4.3 Offer an alpha blocker (alfuzosin, doxazosin, tamsulosin or terazosin) to men with moderate to severe LUTS.
- 1.4.4 Offer an antimuscarinic to men to manage the symptoms of OAB.
- 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).
- 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.
- 1.4.7 Consider offering an antimuscarinic as well as an alpha blocker to men who still have storage symptoms after treatment with an alpha blocker alone.
- 1.4.8 Consider offering a late afternoon loop diuretic* to men with nocturnal polyuria.
- 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.

1.4.10 Do not offer phosphodiesterase-5-inhibitors solely for the purpose of treating lower urinary tract symptoms 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.

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.

1.4.13 Review men taking alpha blockers at 4–6 weeks and then every 6–12 months.

1.4.14 Review men taking 5-alpha reductase inhibitors at 3–6 months and then every 6–12 months.

1.4.15 Review men taking anticholinergics every 4–6 weeks until symptoms are stable, and then every 6–12 months.

* the time of publication (June 2015), loop diuretics (for example, furosemide) did not have a UK marketing authorisation for this indication. Informed consent should be obtained and documented. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

** At the time of publication (June 2015), desmopressin did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

† 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).

Surveillance proposal

These recommendations should not be updated.

Drug treatment

Alpha blockers (ABs)

Previous surveillance summary

The 2012 Evidence update identified an RCT ([Chapple et al. 2011](#)) and a systematic review ([Garimella et al. 2009](#)) that supported the effectiveness of silodosin and naftopidil (neither available in the UK) in treatment of LUTS.

The 2014 review identified evidence on following alpha blockers which all were effective in improving LUTS:

Alfuzosin: 1 cross over RCT (24)

Tamsulosin: 2 systematic reviews (25,26) and 5 RCTs (27–31)

Silodosin: 3 systematic reviews (32–34) and 7 RCTs (35–41)

Doxazosin: 2 RCTs (42,43)

Terazosin: 1 systematic review (44)

2109 surveillance summary

A systematic review and meta-analysis (45) of 9 studies (total n=1,051) compared the efficacy and safety of alpha1-blockers in male patients with acute urinary retention and BPH. Meta-analysis demonstrated that alpha1-blockers significantly improved successful resumption of micturition compared with control. A systematic review and meta-analysis (46) of 17 studies found that alpha1-blockers improved urinary voiding function in patients with benign prostatic obstruction.

Silodosin

An individual patient data meta-analysis (47) of 3 RCTs evaluated the efficacy and safety of silodosin (unavailable in the UK) compared with placebo (n=1494).

Silodosin was more effective than placebo in improving total IPSS, all IPSS-related parameters (storage, voiding, and quality of life item sub-scores), and maximum urine flow rate. Dizziness and orthostatic hypotension incidence rates were similar in silodosin and placebo groups.

A Cochran systematic review (48) of 19 studies (total n=4295) assessed the effects of silodosin for the treatment of LUTS in men with BPH. Silodosin had similar efficacy to that of other alpha blockers (tamsulosin, naftopidil and alfuzosin) but the rate of sexual side effects was higher. The authors concluded that silodosin may reduce urologic symptom scores better than the placebo.

A meta-analysis (49) of 2 RCTs assessed the efficacy and safety of silodosin for treatment of BPH symptoms in 923 patients (mean age 65 years). Compared with placebo, silodosin significantly improved IPSS, obstructive sub-scores and maximum urinary flow rate after 3 to 4 days and sustained for 12 weeks. Silodosin was well tolerated with a low incidence of orthostatic hypotension.

A meta-analysis (50) of 3 RCTs evaluated the efficacy of silodosin on nocturia on 1,266 men with ≥ 2 voids/night at baseline. Silodosin significantly reduced nocturia compared to placebo (53.4 vs. 42.8 %). Silodosin significantly reduced

nocturia within each study and pooled cohort compared to placebo.

An RCT (51) compared the efficacy and safety of silodosin (8 mg once daily) versus tamsulosin (0.4 mg daily) in 53 men with BPH. At 12 weeks, groups remained comparable in terms of IPSS at all visits. Prostate size and uroflowmetry parameters did not change. Both treatments were well tolerated. Sexual dysfunction was encountered only with silodosin and postural hypotension only with tamsulosin.

An RCT (52) assessed the safety and efficacy of silodosin in the management of acute urinary retention related to BPH. A total of 60 men over 50 years of age were equally randomised to either silodosin (8 mg once daily) or placebo for 3 days followed by trial without catheter (TWOC). The success rate of TWOC was 76.7% in the silodosin group and 36.7% in the placebo group. On multivariate analysis, patients in silodosin group had lesser odds of having a failure (0.13) when compared to those not given treatment. There were no adverse effects related to the use of silodosin.

An RCT (53) compared the efficacy and safety profile of tamsulosin (0.4 mg daily), alfuzosin (10 mg daily) and silodosin (8 mg daily) in treatment of LUTS due to BPH. Silodosin improved IPSS and Qmax after 1 week and 3 months of treatment from the baseline. Silodosin improved the quality of life in patients but had more adverse events when compared to tamsulosin and alfuzosin.

An RCT (54) compared the efficacy of tamsulosin (0.4 mg, group A) and silodosin (0.8 mg, group B) in 160 patients suffering from acute urinary retention caused by BPH, planned for trial without catheter. After 3 days of treatment, the catheter was removed, and patients were put on trial without catheter. Patients with a successful trial without catheter were followed up to 2 weeks and one month. Both groups had similar results of trial without catheter (group A: 67.50%, group B 60%). No significant differences were present between group A and group B patients in regard with IPSS, urinary retention measured at the time of successful trial without catheter and during the follow-up.

An RCT (55) compared the efficacy and tolerability of alfuzosin, tamsulosin, and silodosin (not available in the UK) in 90 men with LUTS and BPH. Alfuzosin, tamsulosin, and silodosin showed similar efficacy in improvement of IPSS, QoL, and maximum urine flow rate, with good tolerability, acceptability, and minimum haemodynamic adverse effects.

5-alpha reductase inhibitors (5-ARIs)

[previous surveillance summary](#)

The 2012 Evidence update noted that the US Food and Drug Administration has issued safety advice for 5-alpha reductase inhibitors recommending that urological conditions that mimic BPH (such as prostate cancer) should be ruled out before starting treatment with drugs from this class. This 2012 Evidence update identified following studies on 5-alpha reductase inhibitors:

Dutasteride plus testosterone: 1 RCT
([Page et al. 2011](#))

Finasteride: 1 Cochrane review ([Tacklind et al. 2010](#))

Dutasteride versus finasteride: 1 RCT
([Nickel et al. 2011](#)).

The overall findings suggested that the 5-alpha reductase inhibitors improved urinary symptoms.

The 2014 review identified following studies on 5-alpha reductase inhibitors:

Dutasteride: 2 systematic reviews (56,57)
4 trials (58–61) and 1 RCT(62).

Overall, findings indicated that dutasteride is an effective, safe and well tolerated treatment either as monotherapy or in combination with an alpha blocker

[2109 surveillance summary](#)

A systematic review (63) of 3 studies (21,366 fracture cases) evaluated the association between fractures and exposure to 5-alpha reductase inhibitors or alpha blockers in men with BPH. Exposure to 5-alpha reductase inhibitors was not associated with change in fracture risk but 5-alpha reductase inhibitors had a small protective effect against hip/femur fracture.

A systematic review (64) of 42 RCTs (37 in meta-analysis, total n=23,395) assessed the clinical efficacy and incidence of adverse events associated with 5 alpha reductase inhibitor compared with placebo in symptomatic BPH. A significant improvement was observed following 5-ARIs treatment in all variables (prostate specific antigen (PSA), prostate volume,

International Prostate Symptom Score (IPSS), voiding symptoms of IPSS, maximum urinary flow rate), except in post-void residual volume (PVR) compared with placebo. However, the improvement in PVR, IPSS and maximum urine flow rate was less evident in the more recent publications. Moreover, there was a high risk of adverse events including sexually related complications in the treatment group.

Dutasteride versus finasteride

A systematic review (65) of 4 studies (total n=1,879) compared the efficacy and safety of 5-ARIs (finasteride and dutasteride monotherapy or in combination with an alpha blocker) in improving LUTS. There were no significant differences in need for prostate-related surgery, episodes of acute urinary retention, number of withdrawals due to adverse events, number of patients experiencing serious adverse events and in sexual dysfunction, comparing either as monotherapy or in combination with an alpha blocker.

A systematic review (66) of 21 studies (n=29,094) evaluated the efficacy and safety of dutasteride compared with finasteride, for the treatment of BPH. Dutasteride treatment improved IPSS significantly compared with finasteride treatment (weighted mean difference =1.80). However, the treatment effects of dutasteride compared with finasteride were not significant for peak urinary flow (maximum urine flow rate) and total prostate volume.

Dutasteride

A systematic review (67) of 4 studies (n=12,935) investigated the clinical effectiveness of dutasteride compared with a placebo for treatment of BPH. Dutasteride significantly improved total prostate volume, maximum flow rate, and acute urinary retention however, increased rate of sexual dysfunction.

A meta-analysis (68) of 3 phase III studies (total n=4,321) assessed the impact of dutasteride compared with placebo on nocturia in men with LUTS due to BPH. After 24 months of treatment, reduction in nocturia was significantly better with dutasteride than with placebo across all baseline subgroups tested (mean change in nocturia at 24 months and nocturnal voiding frequency at baseline and study end).

Antimuscarinic drug

previous surveillance summary

The 2012 Evidence update identified a systematic review ([Athanasopoulos et al. 2011](#)) that supported the efficacy of antimuscarinics for treatment of LUTS.

The 2014 review identified a systematic review (69) which reported that combined antimuscarinic and alpha blocker treatment is more effective than monotherapy or placebo in men with overactive bladder. Studies on the following antimuscarinics were also identified in the 2014 review:

Fesoterodine: 5 RCTs (70–74), 2 post-hoc analysis (75,76), 1 economic analysis(77)

Solifenacin: 2 RCTs (78,79)

Propiverine: 1 RCT (80)

Oxybutynin: 1 trial (81)

Trospium chloride: 2 trials (82,83)

Overall findings indicated that antimuscarinics were effective in improving overactive bladder symptoms in men.

2109 surveillance summary

Studies on following antimuscarinic were identified in current review:

Fesoterodine

An RCT (84) assessed the efficacy and safety of fesoterodine (4 mg daily could increase to 8 mg) in 794 men aged 65 and older with overactive bladder. At week 12, the fesoterodine group had greater improvement in urgency episodes, micturition, nocturnal micturition, incontinence pad use, and OAB (overactive bladder) Questionnaire scores but not in urgency urinary incontinence episodes compared with placebo.

An RCT (85) assessed the efficacy and safety of fesoterodine (8 mg daily) versus placebo in 609 men who responded sub-optimally to tolterodine extended release (ER) 4 mg daily. At week 12 of treatment, participants receiving fesoterodine had significantly greater improvement from baseline versus placebo in urgency urinary incontinence episodes, urgency episodes and scores on the Patient Perception of Bladder Control, Urgency Perception Scale and OAB Questionnaire Symptom, and health-related Quality of Life (QoL) scales. Compared with placebo, the intervention group had 4 times and 3 times higher rate

of dry mouth and constipation respectively.

An RCT (86) compared the efficacy of fesoterodine or mirabegron add-on therapy for persistent overactive bladder symptoms despite silodosin monotherapy (an alpha blocker unavailable in the UK), in 120 men with LUTS and BPH. At 12 weeks of treatment, adding fesoterodine to silodosin was more effective than adding mirabegron to silodosin in improving overactive bladder symptoms and storage functions, without deteriorating voiding symptoms or sexual functions.

Imidafenacin, Propiverine, Oxybutynin patch

An RCT (87) assessed the efficacy and safety of imidafenacin (0.1 mg twice daily; an antimuscarinic not currently available in the UK- group A) compared with propiverine (20 mg once daily- group B) for treatment of overactive bladder in 162 men. At 12 weeks, all overactive bladder symptoms and quality of life was improved in group A. Imidafenacin was not inferior to propiverine for reduction of urgency urinary incontinence episodes and was better tolerated than propiverine in the safety profile (the severity of dry mouth was significantly less in the group A than in group B).

An RCT (88) evaluated the efficacy and safety of once daily oxybutynin patch, propiverine or placebo therapy compared with placebo in 1,530 men with overactive bladder. The change of the mean daily frequency of micturition from baseline was significantly improved in oxybutynin patch group compared with placebo. There was

no significant difference in the mean daily number of micturitions between the oxybutynin patch and propiverine group. The incidence of dry mouth and constipation was higher with propiverine than with the oxybutynin patch or placebo. Application site mild dermatitis was more frequent with the oxybutynin patch (31.8%) than with propiverine (5.9%) or placebo (5.2%).

Tolterodine

A systematic review (89) of 19 studies evaluated the efficacy and tolerability of tolterodine. The findings from 1,529 patients with overactive bladder showed 71% mean reduction in urgency incontinence episodes in the tolterodine extended release group compared to a 60% reduction in the tolterodine immediate release. Tolterodine in comparison with other antimuscarinic drugs was more effective than placebo in reducing micturition/24 h, urinary leakage episodes/24 h, urgency episodes/24 h, and urgency incontinence episodes/24 h. Dry mouth and constipation were the most frequently reported adverse events.

An RCT (90) compared the efficacy of first line antimuscarinic and alpha blocker monotherapy in 163 men with storage lower urinary tract symptoms. Participants were randomised to receive tolterodine 4 mg or doxazosin 4 mg daily for 12 weeks. The rate of improved outcome (IPSS, quality of life index) was similar in first line tolterodine and doxazosin monotherapy.

Phosphodiesterase 5 inhibitors (PDE5Is)

Previous surveillance summary

No new evidence was identified at the 2012 Evidence update. The 2014 review identified 5 RCTs (91–98), 1 meta-analysis (99) and 2 post-hoc analyses (100,101) that suggested, PDE5Is are an effective treatment for LUTS.

2109 surveillance summary

A Cochrane systematic review (102) of 16 RCTs examined the effects of PDE5Is compared to placebo and other standard of care drugs (alpha blockers and 5-ARIs) in men with LUTS and BPH. Compared to placebo, PDE5Is reduced IPSS total and Benign Prostatic Hyperplasia Impact Index (BPHII) scores, with small increase in adverse events. PDE5Is and alpha blockers were similar in improving IPSS total, BPHII, and incidence of alpha blockers. Urinary symptoms were equally improved in PDE5Is combined with alpha blockers compared with PDE5Is or alpha blockers alone or PDE5Is combined with 5-ARI compared with 5-ARI alone.

A meta-analysis (103) of 28 studies (total n=19,820) investigated the real benefit and safety of PDE5Is for BPH and LUTS. The overall weighted mean differences of total IPSS, voiding IPSS, storage IPSS, and QoL showed significant improvement from the baseline following PDE5Is treatment.

Tadalafil

A systematic review (104) of 8 systematic reviews evaluated effectiveness of PDE5Is in improving LUTS. PDE5Is improved IPSS with small change in flow rate compared with placebo (Maximum urine flow rate

mean difference vs placebo: 0.01-1.43). Pooled data analyses revealed that tadalafil 5 mg once daily improved LUTS and nocturnal voiding frequency.

A meta-analysis (105) of 3 RCTs evaluated the efficacy and safety of tadalafil 5 mg daily in men with LUTS. Tadalafil 5 mg led to great improvement in all IPSS at 4, 8- and 12-week timepoints compared with placebo. Tadalafil efficacy was similar between patient subgroups of varied disease severity, prior alpha blocker use, and prostate volume. The drug was slightly less effective in older men. No unexpected adverse events were reported.

An RCT (106) evaluated the efficacy, safety and tolerability of tadalafil 5 mg once daily in men with LUTS and BPH. A greater improvement was observed in total IPSS, voiding and storage IPSS, Quality of Life Index Score, Patient and Clinician Global Impressions of Improvement from baseline to study endpoint (weeks 4, 8 and 12) versus placebo. No safety concerns were identified.

An RCT (107) evaluated the effect of tadalafil on LUTS storage and voiding IPSS sub-scores in 1,499 men. Tadalafil improved both storage and voiding symptoms during the 12-week study period. The severity of storage dysfunction before treatment did not affect the response to the treatment.

An RCT (108) investigated the efficacy and safety of tadalafil versus solifenacin (an antimuscarinic) in 75 men with LUTS. The change in the amount of residual urine volume was significantly larger in the solifenacin than tadalafil-treated group;

lower urinary tract symptoms and uroflowmetry measures, did not differ significantly between the two groups. Seven (18%) and 12 (32%) patients in the tadalafil and solifenacin groups, respectively, discontinued treatment because of adverse events.

An RCT (109) assessed the treatment satisfaction with tadalafil or tamsulosin (an antimuscarinic) versus placebo in 12 weeks in 172 men with LUTS and BPH. Treatment satisfaction was greater with tadalafil vs placebo, with no significant difference between tamsulosin and placebo.

An RCT (110) compared the differential effects of tadalafil and tamsulosin in 40 men with BPH using a cross over study design. All patients received a placebo lead-in period for 2 weeks, followed by an active drug for 6 weeks; placebo wash out for 4 weeks and then crossed over to second active drug for another 6 weeks. Both tadalafil and tamsulosin improved total IPSS score, quality of life and erectile function and those patients who did not respond to one drug showed improvement with the other.

General

A systematic review (111) of 23 studies (total n=1044) evaluated the urodynamic outcomes of alpha-1 adrenergic antagonists (Alpha blockers), 5-alpha reductase inhibitors (5-ARIs), PDE5Is, and phytotherapeutic compounds in patients with lower urinary tract symptoms related to benign prostatic obstruction. Alpha blockers and 5-ARIs improved bladder outlet obstruction index, detrusor pressure

at maximum urinary flow rate. PDE5Is and phytotherapeutic compounds had no great effects on urodynamic parameters.

Hormones

Desmopressin

Previous surveillance summary

The 2012 identified an RCT ([Wang et al. 2011](#)) which reported that low dose desmopressin is an effective and safe treatment for nocturia in men aged ≥ 65 years with BPH.

The 2014 review identified 2 RCTs (112,113) which found desmopressin significantly decreased nocturia in men with BPH. A further RCT (114) identified in 2014 review reported improvements in quality of life following desmopressin treatment.

2109 surveillance summary

A Cochrane systematic review (115) of 14 RCTs (n=2966) assessed the effects of desmopressin as compared to other interventions in the treatment of nocturia in men. The authors concluded that desmopressin reduced the number of nocturia compared with placebo over 3 to 12 months follow-up with no increase in major adverse events. The reduction in nocturia was similar to that with alpha blockers. Desmopressin was well tolerated and significantly increased the health-related quality of life and sleep quality.

An RCT (116) investigated the efficacy and safety of desmopressin (0.2 mg for 8 weeks) add-on therapy for 86 men with LUTS and persistent nocturia despite alpha blocker therapy. Compared with placebo,

desmopressin significantly improved nocturia, nocturnal urine volume, total IPSS, the nocturnal polyuria index and ICIQ-N (International Consultation on Incontinence Questionnaire-Nocturia), and patient willingness to continue with treatment. The incidence of adverse events in the desmopressin was similar between groups.

Non-steroidal anti-inflammatory drugs (NSAIDs)

[Previous surveillance summary](#)

No new evidence was identified at the 2012 Evidence update. The 2014 review identified a systematic review (117) which evaluated the safety and long-term impact of NSAIDs use in men with BPH and indicated that NSAIDs improved IPSS.

[2109 surveillance summary](#)

No relevant evidence was identified.

Beta 3-adrenoceptor agonist

[Previous surveillance summary](#)

Mirabegron vs placebo

No new evidence was identified at the 2012 Evidence update. The 2014 review identified 5 RCTs (118–122), a systematic review (123) and pooled data from 3 RCTs (124) that indicated mirabegron improved LUTS compared with placebo.

Mirabegron versus tolterodine

No new evidence was identified at the 2012 Evidence update. The 2014 review identified an RCT (125) which assessed 12-month safety and efficacy of mirabegron compared with tolterodine (an antimuscarinic) for overactive bladder.

Both treatments improved key overactive bladder symptoms from the first measured time point of 4 weeks, and efficacy was maintained throughout the 12-month treatment period.

[2019 surveillance summary](#)

No relevant evidence was identified.

Selective serotonin and norepinephrine reuptake inhibitor (SNRI) antidepressants

[Previous surveillance summary](#)

Duloxetine

No new evidence was identified at the 2012 Evidence update. The 2014 review identified an RCT (126) which compared duloxetine with placebo in men with stress urinary incontinence after radical prostatectomy. The frequency of incontinence episodes was significantly reduced with duloxetine compared with placebo and duloxetine improved quality of life.

Nitrate

No new evidence was identified at the 2012 Evidence update. The 2014 review identified an RCT (127) which compared sublingual isosorbide dinitrate with placebo in men with acute urinary retention indicating that the mean voided urine volume was greater in the intervention group compared with control.

[2019 surveillance summary](#)

No relevant evidence was identified.

Combination therapy

Alpha blockers combination therapy

Alpha blockers plus antimuscarinics compared with alpha blockers alone

Please see “Antimuscarinic combination therapy” for this combination.

Alpha blockers plus 5-alpha reductase inhibitors (5-ARI) versus alpha blockers or 5-ARI

Tamsulosin and dutasteride combination versus monotherapy

previous surveillance summary

The 2012 Evidence update identified an RCT ([Roehrborn et al. 2010](#)) which found tamsulosin and dutasteride combination therapy is more effective than either drug as monotherapy in improving the urinary retention, decreasing risk of acute urinary retention and need for surgical intervention.

2019 surveillance summary

An RCT (128) assessed the effectiveness and safety of tamsulosin 0.2 mg plus dutasteride 0.5 mg combination compared with tamsulosin 0.2 mg in 607 men with moderate to severe BPH. Combination therapy reduced IPSS score at month 24, improved peak urinary flow at every assessment and reduced prostate volume at months 12 and 24 better than the monotherapy. Combination therapy was also associated with a reduction in the risk of acute urinary retention or BPH related surgery.

Tamsulosin plus finasteride versus Tamsulosin

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance summary

An RCT (129) compared tamsulosin plus finasteride (combination therapy) and tamsulosin (monotherapy) after a trial period of 6 months in 92 men with BPH. The total American Urological Association symptom score and residual urine volume were improved significantly in the combination group compared with monotherapy.

An RCT (130) assessed the efficacy of tamsulosin and finasteride as monotherapy and in combination in men with BPH. At 6-month follow-up, tamsulosin monotherapy and combination therapy appeared to be equally effective in improving IPSS score and peak urinary flow rate while finasteride monotherapy appeared to be the least effective. Side effects were more in patients taking finasteride alone or as combination therapy.

Tamsulosin and finasteride plus omega-3 fatty acids versus tamsulosin and finasteride

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance summary

An RCT (131) assessed whether combination therapy with omega-3 fatty acids, and tamsulosin plus finasteride offers an advantage compared with tamsulosin plus finasteride therapy in patients with BPH. Both treatments

equally improved IPSS, Q max and prostate volume from baseline at follow-up. Omega-3 fatty acids plus tamsulosin and finasteride showed higher improvement in IPSS, and Q max, at the 1, 3 and 6-month interval. Prostate volume in the study group also showed more improvement at 6-month follow-up. Adverse effects were the same in both groups during the study.

Tamsulosin and dutasteride vs dutasteride

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance summary

A systematic review (132) of 9 studies evaluated the efficacy and safety of dutasteride, alone or in combination with tamsulosin, compared with placebo for the treatment of BPH. Dutasteride was superior to placebo in improving IPSS, peak urinary flow (Q max), and change in total prostate volume while it resulted in more frequent drug-related adverse events (RR=1.35). Combination therapy with dutasteride and tamsulosin resulted in significantly greater improvements in IPSS and Q max compared with tamsulosin monotherapy.

General

Previous surveillance summary

From the 2014 review, one RCT (133) indicated that alpha blocker plus 5-alpha reductase inhibitor combination therapy has improved LUTS compared with monotherapy among men with BPH.

Two studies (134,135) compared alpha blocker monotherapy with combination

therapy involving an alpha blocker and a 5-alpha reductase inhibitor for BPH.

Combination therapy resulted in significant improvements in LUTS. However, one RCT (96) indicated when treatment was given for <1-year, alpha blockers alone were just as effective.

2019 surveillance summary

A systematic review (136) of 5 RCTs (n=6,131) evaluated the impact of combination therapy with alpha blockers and, 5-alpha reductase inhibitors (5-ARI) on the risk of erectile dysfunction (ED). Combination therapy with alpha blockers and 5-ARIs was associated with higher risk of ED compared with monotherapy.

Alpha blockers plus PDE5 inhibitor versus alpha blocker or PDE5 inhibitor

Previous surveillance summary

Four RCTs (137–140) from the 2014 review indicated that combination therapy with an alpha blocker and a PDE5 inhibitor improved LUTS compared with monotherapy with an alpha blocker.

Evidence from 2014 review also indicated that following combinations have a beneficial effect on LUTS compared with monotherapy:

Doxazosin and sildenafil versus sildenafil: 1 RCT (141)

Tamsulosin and vardenafil versus tamsulosin: 1 RCT (142)

Tamsulosin and dutasteride versus tamsulosin: 5 studies (4 RCTs and 2 post-hoc analyses) (143–148)

Tamsulosin and tadalafil versus tamsulosin: 2 RCTs (139,140)

Evidence from 2014 review on following combination reported that the following combination therapies are no more effective than monotherapy or placebo:

Alpha blockers and tadalafil versus placebo: 1 RCT(149)

Alfuzosin and sildenafil versus alfuzosin: 1 RCT(150)

2019 surveillance summary

Tamsulosin and sildenafil versus tamsulosin

An RCT (151) compared tamsulosin and sildenafil in combination with tamsulosin alone for management of acute urinary retention in 101 patients with BPH. At 3-month follow-up, combination therapy did not improve urinary retention more than tamsulosin alone.

Tamsulosin plus Xipayimaizipizi versus tamsulosin

One RCT (152) evaluated the efficacy of the combination therapy of tamsulosin 0.2 mg plus Xipayimaizipizi (not available in the UK) at 500 mg versus tamsulosin 0.2 mg in treatment of LUTS due to BPH in 60 men. After 4 weeks treatment, the combination group showed more improvement than the monotherapy group in nocturnal urination frequency, IPSS and maximum urine flow rate, and QoL. Adverse reactions were found more in the combination group compared with the monotherapy group (16.6% vs 10% respectively).

Tamsulosin and tadalafil versus tamsulosin

One RCT (153) compared monotherapy with tamsulosin or tadalafil and their combination in 183 men with BPH. Participants were divided equally to 3 groups: group A received 20 mg daily tadalafil; group B received 0.4 mg daily tamsulosin; group C received a combination of 0.4 mg/daily tamsulosin and 20 mg/daily tadalafil. Combination treatment significantly improved IPSS, international index of erectile function questionnaire scores and maximum urine flow rate compared with group A and B.

Tamsulosin and tadalafil versus tamsulosin or tadalafil alone

An RCT (154) evaluated the combination of tamsulosin and tadalafil compared with tamsulosin or tadalafil alone in 133 men with LUTS due to BPH. Tamsulosin and tadalafil, either alone or in combination, equally improved LUTS.

Alfuzosin and tadalafil versus each monotherapy

An RCT (155) evaluated alfuzosin and tadalafil as monotherapy and in combination in 50 patients with LUTS and BPH. Compared with monotherapy, combination therapy significantly improved IPSS scores and post-void residual urine volume. Combination therapy was similar to alfuzosin monotherapy in improving maximum urine flow rate.

Tamsulosin and sildenafil versus tamsulosin

An RCT (156) evaluated adding sildenafil citrate to tamsulosin in the treatment of

lower urinary tract symptoms due to benign prostatic hyperplasia (LUTS/BPH) in men with or without erectile dysfunction. Sildenafil citrate plus tamsulosin improved LUTS, erectile function, and patient QoL more than tamsulosin.

General

A systematic review (157) of 11 RCTs (total n=855) evaluated the efficacy of alpha blockers with or without phosphodiesterase type 5 inhibitors (PDE5-Is) in patients with LUTS/BPH. Combination therapy greatly improved IPSS, maximum urine flow rate, and sexual function in patients with LUTS/BPH.

A systematic review (158) of 12 studies compared alpha blockers and phosphodiesterase 5 inhibitors used alone or combined for the treatment of LTUS due to BPH. Combination and monotherapy were equally effective in improving LUTS/BPH. PDE5Is monotherapy was less effective in reduction of PVR than alpha blockers only.

A metanalysis (159) of 10 studies (total n= 616) evaluated efficacy of alpha-1-adrenergic blockers alone and in combination with long- and short-acting PDE5-Is in LUTS. Combination of an PDE5I and alpha-1-adrenergic blocker was the most the effective treatment in improving IPSS and maximum urine flow rate.

Other Alpha blockers combination therapy

[previous surveillance summary](#)

No relevant evidence was identified.

[2019 surveillance summary](#)

Tamsulosin and desmopressin versus tamsulosin

An RCT (160) evaluated efficacy and safety of adding low dose oral desmopressin to tamsulosin therapy for treatment of nocturia in 248 men with BPH. The frequencies of night voids decreased by 64.3% in the combination group compared with 44.6% in tamsulosin group. IPSS, QoL score, post-void residual urine volume and maximum urine flow rate were improved equally in both groups.

A systematic review (161) of 18 studies (total n=3,072) evaluated the effect of oral desmopressin (dose range from 0.05 mg to 0.4 mg at bedtime) in patients with nocturia associated with BPH. There was a significant 43% reduction in nocturia with desmopressin alone. Combined Alpha blockers and desmopressin lead to a decrease in the frequency of night voids by 64.3% compared to 44.6% when using alpha blockers only. The incidence of hyponatraemia associated with desmopressin use was 4.4-5.7%.

Tamsulosin and ketoconazole versus tamsulosin

An RCT (162) investigated tamsulosin in combination with ketoconazole in acute urinary retention due to BPH in 106 men. The treatments were well tolerated by all patients and the incidence of the successful trial without catheter was higher in the combined treatment group (77.35%) compared with the tamsulosin group (58.84%). [Doxazosin plus Longbishu Capsule \(LBS\)](#)

An RCT (163) investigated the effect of Longbishu Capsule (LBS, a Chinese medicine not available in the UK), doxazosin, and combination therapy in 360 men with BPH who were assigned to: group A (LBS placebo plus doxazosin), group B (LBS plus doxazosin) or group C (LBS plus doxazosin placebo). After 12-month treatment, all 3 groups showed improvements in IPSS and maximum urinary flow rate from baseline. However, the post-void residual urine volume decreased more in group B and C compared with group A. Adverse events were similar in the 3 groups.

General

Previous surveillance summary

No new evidence was identified.

2019 surveillance summary

A systematic review and network meta-analysis (164) of 66 RCTs (total n=29,384) compared the efficacy of different drug therapies for LUTS due to BPH. Alpha blockers plus phosphodiesterase 5 inhibitors (PDE5Is) achieved greatest improvements in IPSS total score, IPSS storage and IPSS voiding. The combination of alpha blockers plus 5alpha-reductase inhibitors was the best for increasing maximum urinary flow rate (Maximum urine flow rate) compared with placebo. Alpha blockers plus antimuscarinics were ranked second for reduction of IPSS storage; monotherapies including antimuscarinics showed no effect on this aspect. Additionally, PDE5Is alone showed highest effectiveness for LUTS/BPH except maximum urine flow rate.

PDE5Is plus 5-alpha reductase inhibitor (5-ARI)

Tadalafil and finasteride

Previous surveillance summary

An RCT (165) identified in the 2014 review investigated tadalafil co-administered with finasteride over 26 weeks. The results indicated that co-administration of tadalafil and finasteride provided early LUTS improvement in men with BPH and prostatic enlargement.

2019 surveillance summary

This section was updated in 2015 and new recommendation was added subsequently: 'Do not offer phosphodiesterase-5-inhibitors solely for the purpose of treating lower urinary tract symptoms in men, except as part of a randomised controlled trial (1.4.10).

One RCT (166) assessed tadalafil 5 mg co-administered with finasteride 5 mg during 26 weeks on LUTS in 695 men. The improvements in IPSS, IPSS storage and voiding after 4, 12 and 26 weeks of tadalafil and finasteride co-administration were greater than in the placebo group. Tadalafil and finasteride co-administration was well tolerated, and most adverse events were mild/moderate.

A second RCT (167) assessed the treatment satisfaction and clinically meaningful improvements comparing co-administration of tadalafil 5 mg with finasteride 5 mg versus finasteride alone in 695 men with prostatic enlargement secondary to BPH. Treatment satisfaction at week 26 was greater with tadalafil/finasteride compared with

placebo/finasteride for total treatment satisfaction scale score and satisfaction with efficacy sub-score; scores were not significantly different between treatments in satisfaction with dosing or side effects.

Antimuscarinic combination therapy

Previous surveillance summary

In the 2012 review, one RCT ([Yamaguchi et al. 2011](#)) evaluated adding solifenacin (an antimuscarinic) to tamsulosin. There were significantly greater improvements in urinary symptoms in the combination group compared with monotherapy.

Evidence from 2014 review supports the efficacy and safety of following antimuscarinics combination with alpha blockers in treating men with LUTS:

Trospium chloride and terazosin versus terazosin and placebo: 1 RCT (168)

Propiverine and terazosine versus terazosin and placebo: 1 RCT (169)

Tolterodine and Alpha blockers and/or 5-alpha reductase inhibitors versus tolterodine: 1 RCT (170)

Imidafenacin and tamsulosin versus tamsulosin: 3 systematic reviews (171–173), 1 RCT (174), 1 trial (175)

Solifenacin and tamsulosin versus placebo or tamsulosin: 5 RCTs (176–180)

Fesoterodine and tamsulosin versus tamsulosin: 2 RCTs (181,182)

Tolterodine and tamsulosin versus tolterodine or tamsulosin: 1 study (183)

based on the UK healthcare setting indicated that tolterodine plus tamsulosin

combination therapy appeared to be cost effective compared with tolterodine or tamsulosin monotherapy or placebo in men with LUTS.

2019 surveillance summary

Propiverine plus silodosin plus versus silodosin

An RCT (184) evaluated long-term efficacy and safety of a combination therapy (propiverine 20 mg/day plus silodosin 8 mg/day) and monotherapy (silodosin 8 mg/day) in 120 men with BPH and voiding and overactive bladder symptoms. The combination group showed significant improvement in IPSS-QoL, and overactive bladder urgency score at 1-year evaluation compared with monotherapy. In storage function, both groups showed improvements, but the combination therapy demonstrated significant improvement in terms of disappearance rate of detrusor overactivity and bladder capacity.

Antimuscarinic plus alpha blockers versus alpha blocker or antimuscarinic monotherapy

A Cochrane systematic review (185) of 18 RCTs (total n=4,084) compared combinations of antimuscarinics and alpha blockers with alpha blocker monotherapy in patients with moderate to severe LUTS. Compared with monotherapy group, significant improvement was reported for storage IPSS, quality of life score, micturition per 24 hours, and urgency episodes per 24 hours in the combination therapy group. The 2 groups were similar regarding maximum flow rate, Total International Prostate Symptom Score

(TIPSS) and Voiding International Prostate Symptom Score (VIPSS). However, post-void residual volume, was worse in the combination therapy group.

A metanalysis (186) of 16 studies (total n=3,548) evaluated initial combination treatment of an alpha blocker plus antimuscarinic compared with alpha blocker monotherapy in LUTS. Compared with monotherapy, the combination therapy significantly improved IPSS, QoL and maximum urine flow rate. The number of acute urinary retention events or post-voided residual volume were comparable between the combination treatment and monotherapy.

An RCT (187) assessed adding an antimuscarinics or antidiuretic agent to an alpha blocker for improving LUTS and nocturia in 405 men previously treated with an alpha blocker. Adding an antimuscarinic agent or antidiuretic agent significantly improved LUTS and nocturia at 4, 8 and 12-weeks assessment compared with a single antimuscarinic agent alone.

An RCT (188) evaluated the efficacy and safety of combination therapy of a short-acting antimuscarinic, imidafenacin and an alpha blocker compared with monotherapy with an alpha blocker in 221 men with LUTS and storage symptoms. Micturition number per 24 hours, daytime frequency, urgency, IPSS-QoL score improved greater in the combination therapy group, but changes in total IPSS, nocturia episodes, and safety outcomes were similar in 2 groups.

Solifenacin and tamsulosin and versus tamsulosin

Findings from an RCT (189) indicated that a once daily fixed-dose combination of solifenacin and tamsulosin was associated with consistent improvements in QoL compared with placebo and tamsulosin monotherapy in men with LUTS and BPH.

An RCT (190) evaluated the combination of solifenacin with tamsulosin oral controlled alpha blockers absorption system (OCAS; a drug delivery refinement that incorporates a matrix of gel-forming and gel-enhancing agents) versus tamsulosin alone for the treatment of 937 men with LUTS. Combination therapy was associated with significant improvements in micturition frequency, voided volume and QoL compared with tamsulosin. However, combination therapy did not improve IPSS compared with tamsulosin OCAS monotherapy in men with both voiding and storage symptoms at baseline. Combination therapy was well tolerated.

An RCT (191) evaluated the efficacy and safety of the combination of tamsulosin and solifenacin in 166 men with BPH and overactive bladder. Combination therapy showed a better effect than tamsulosin only in overactive bladder symptom score but there were no significant differences for IPSS, maximum urine flow rate, routine urine test results, and adverse effects.

An RCT (192) evaluated initial combined therapy of tamsulosin 0.2 mg and solifenacin 5.0 mg daily compared with tamsulosin 0.2 mg daily in 150 men with BPH and overactive bladder. At 4 weeks, IPSS total score and voiding symptom

score, were similar in the 2 groups but the IPSS storage symptom score was significantly lower in the combination therapy group. At 12 weeks, IPSS storage symptom score were similar in 2 groups.

An RCT (193) evaluated combination therapy of solifenacin and tamsulosin for up to 1 year in 1,208 men with both storage and voiding symptoms. A fixed-dose combination of solifenacin and tamsulosin oral controlled alpha blockers absorption system was associated with a low rate of urinary retention and acute urinary retention compared with placebo.

Imidafenacin (antimuscarinic not available in the UK) and tamsulosin (alpha blocker) and dutasteride (5-ARI) versus tamsulosin and dutasteride

An RCT (194) examined the long-term efficacy of combination of tamsulosin 0.2 mg plus dutasteride 0.5 mg plus imidafenacin 0.2 mg (TDI) therapy compared with tamsulosin plus dutasteride (TD) therapy in 163 men with BPH and a prostate volume ≥ 30 mL who remained with overactive bladder symptoms despite tamsulosin monotherapy for ≥ 8 weeks. There were decreases in the overactive bladder Symptom Score and IPSS storage score compared with baseline in the TDI versus TD group at week 52, but the change in the total IPSS were similar between the 2 groups. There was no change in PVR from week 24 to week 52 in either groups.

Imidafenacin (antimuscarinic not available in the UK) and tamsulosin (alpha blocker) and dutasteride (5-ARI) versus tamsulosin and dutasteride monotherapy.

An RCT (195) evaluated the efficacy and safety of a combination therapy with dutasteride and imidafenacin in 163 men with BPH and persistent overactive bladder symptoms. Tamsulosin, dutasteride and imidafenacin combination therapy significantly improved overactive bladder symptoms and quality of life without causing serious adverse drug reactions in patients with enlarged prostate not responding to tamsulosin. Tamsulosin, dutasteride and imidafenacin combination therapy improved total IPSS at 24 weeks compared with the tamsulosin and dutasteride monotherapy. The storage IPSS, quality of life, and benign prostatic hyperplasia impact index also improved significantly in the combination therapy group compared with the tamsulosin and dutasteride monotherapy.

Tamsulosin and solifenacin and versus placebo or tamsulosin

A meta-analysis (196) of 7 studies evaluated tamsulosin and solifenacin combination therapy compared with tamsulosin monotherapy for men with LUTS. Combination therapy significantly improved storage IPSS, quality of life, micturition per 24 hours and urgency episodes per 24 hours compared with monotherapy. The incidence of adverse effects and maximum urine flow rate in the tamsulosin and solifenacin combined therapy group (30.82%) was similar for the tamsulosin monotherapy groups (25.75%).

An RCT (197) evaluated the efficacy of initial combined treatment of alpha blocker plus dose-dependent antimuscarinic agent (tamsulosin 0.2 mg plus solifenacin 5 mg daily) compared with the alpha blocker monotherapy (tamsulosin 0.2 mg daily) in 146 men with BPH and overactive bladder. Combined use of tamsulosin and solifenacin showed greater improvement in storage symptoms compared with tamsulosin monotherapy. Dry mouth (17%), acute urinary retention (4%) were reported in the combination treatment group.

Propiverine and alfuzosin versus alfuzosin

An RCT (198) assessed the efficacy and safety of treatment with alfuzosin plus propiverine in 135 men with LUTS and an overactive bladder. Patients received alfuzosin 10 mg alone (Group A) or with propiverine 10 mg (Group B) or 20 mg (Group C) for 8 weeks. The improvement of overactive bladder scores in Group C was greater than Group A and B. Maximum urine flow rate and PVR were comparably improved in the 3 groups. Overall adverse event rates were higher in Group C.

Tolterodine extended release (ER) plus tamsulosin versus ER monotherapy

An RCT (199) evaluated the efficacy and safety of medium to long-term use of tolterodine extended release (ER) with or without tamsulosin in 152 men with BPH and prostate volume ≥ 25 . Compared with placebo, tolterodine ER plus tamsulosin greatly improved total IPSS, storage IPSS, voiding IPSS, QoL, maximum urine flow rate, and post-void residual volume at

weeks 4, 12, and 24. Continued treatment did not increase adverse events.

Tolterodine ER alone did not improve total IPSS, voiding IPSS, QoL, or maximum urine flow rate, compared with placebo.

Non-steroidal anti-inflammatory drugs (NSAIDs) plus alpha blockers

Previous surveillance summary

Celecoxib and terazosin versus terazosin

The 2014 identified one RCT (200) which compared celecoxib plus terazosin with terazosin in men with BPH and found that the overall severity of symptoms, irritative symptoms, and prostate volume decreased more in the combined treatment group than in the control group.

2019 surveillance summary

Meloxicam plus tamsulosin hydrochloride vs tamsulosin hydrochloride

An RCT (201) compared the effect of combined therapy of tamsulosin hydrochloride plus meloxicam, with tamsulosin hydrochloride alone in 400 men with BPH. Tamsulosin hydrochloride plus meloxicam, improved average urinary flow rates significantly compared with the monotherapy.

Beta 3-adrenoceptor agonist combination therapy

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance summary

Mirabegron plus tamsulosin versus tamsulosin

An RCT (202) evaluated the efficacy and safety of add-on treatment with a beta3-adrenoceptor agonist (mirabegron) for overactive bladder symptoms in 94 men with benign prostatic obstruction who were nonresponsive to alpha1-blocker (tamsulosin) treatment. The changes in scores for urinary urgency, daytime frequency, IPSS storage symptom and quality of life index at 8 weeks were greater in the combination group than in the monotherapy group. The change in post-void residual urine volume was also greater in the combination group. Six patients in the combination group had adverse events reported.

Mirabegron plus solifenacin (antimuscarinic) versus solifenacin

An RCT (203) investigated improvements in overactive bladder and patient reported outcomes in 2,174 patients with overactive bladder and refractory incontinence treated with mirabegron 50 mg plus solifenacin 5 mg daily versus solifenacin 5 or 10 mg daily. More patients on the combination treatment achieved clinically meaningful improvements in incontinence and micturition frequency. Improvements were accompanied by similar improvements in Patient Perception of Bladder Condition, symptom bother and health-related quality of life.

An RCT (204) evaluated the efficacy and tolerability of combination therapy (mirabegron 50 mg daily and solifenacin 5 mg daily) versus monotherapy (solifenacin

5 or 10 mg daily) in 2,174 men with overactive bladder who remained incontinent despite initial solifenacin 5 mg treatment. Combination therapy further improved overactive bladder symptoms (incontinence and frequent urination) versus solifenacin 5 or 10 mg monotherapy and was well tolerated.

Vibegron and tolterodine versus vibegron or placebo

A phase IIb RCT (205) assessed the efficacy and tolerability once daily oral vibegron when administered alone or along with tolterodine in 1,395 men with overactive bladder. From baseline to week 8, vibegron monotherapy (50 and 100 mg daily) significantly decreased average daily micturition and the number of urge incontinence episodes compared with placebo. Vibegron was well tolerated as monotherapy and combined with tolterodine.

Intelligence gathering

Topic experts highlighted the following:

- 'There is insufficient warning about the potential for cognitive decline with antimuscarinic drugs (1.4.8) (These have been reviewed as part of the Female UI guideline (awaiting publication) so there is little point in carrying out the same searches.)'
- 'There is new evidence of combination therapy with solifenacin and mirabegron and combination of mirabegron and solifenacin.'
- 'There is a poor persistence and compliance with antimuscarinic

therapy in overactive bladder. This calls for second line therapy with a different class agent like mirabegron. However, cost benefit analysis with persistence has not been studied fully to make mirabegron as a first line agent. Therefore, no change is needed at this point.'

Impact statement

Alpha blockers

Evidence from an RCT and a systematic review identified in 2012 Evidence update supported the effectiveness of silodosin and naftopidil in treatment of LUTS. The studies concluded that silodosin has efficacy comparable to, but without additional benefits over, tamsulosin however, because silodosin is not available in the UK there is no impact on recommendations in the guideline,

The 2014 review identified evidence in favour of following alpha blockers: ifuzosin, tamsulosin, silodosin, doxazosin and erazosin for improving LUTS. The evidence is unlikely to impact the guideline recommendations as alfuzosin, tamsulosin, doxazosin and terazosin are already recommended for men with moderate to severe LUTS and silodosin is not currently licensed for use in the UK.

New evidence in current review from 2 systematic review suggests that alpha1-blockers in general appear to improve urinary voiding function in patients with benign prostatic obstruction and this is in line with the current recommendation that recommends alpha blockers for treatment of moderate to severe LUTS.

New evidence from 4 systematic reviews and 5 RCTs indicates that silodosin improved IPSS but had an adverse effect on sexual function in men. Silodosin is not currently licensed for use in the UK.

5-alpha reductase inhibitors

The overall findings from 2012 suggested that 5-alpha reductase inhibitors improve urinary symptom. The findings from 2014 review indicated that dutasteride is an effective, safe and well tolerated treatment either as monotherapy or in combination with an alpha blocker. Findings from 5 systematic reviews and 1 meta-analysis in current 2019 review also support the use of 5-alpha reductase inhibitors in improving LUTS. This reinforces current recommendations in NICE GC97, which propose 5-alpha reductase inhibitors but do not indicate a preferred drug in this class.

There is a warning on [Finasteride: rare reports of depression and suicidal thoughts](#) from the 2017 Medicines and Healthcare products Regulatory Agency (MHRA). Mood alterations including depressed mood, depression and, less frequently, suicidal ideation have been reported in patients treated with finasteride 5 mg. This has no impact on current recommendations but should be considered if the guideline is updated.

Antimuscarinic drug

The 2012 Evidence update identified a systematic review that supported the efficacy of antimuscarinics for treatment of LUTS. The 2014 review identified 2 systematic reviews that indicated that combined antimuscarinic with alpha

blocker treatment is generally more effective than monotherapy or placebo in men with overactive bladder.

According to the Evidence Update from 2012 review, these drugs are now referred to as antimuscarinics. The Evidence Update from 2012 review concluded that the reviews supports the recommendations in the guideline which suggest offering antimuscarinics (referred to as anticholinergics in the guideline) to men with overactive bladder, and combination treatment with alpha blockers and antimuscarinics for those with persisting storage symptoms.

Studies on the following antimuscarinics were identified in current review:

Fesoterodine (3 RCTs), imidafenacin, propiverine, oxybutynin patch (2 RCTs), tolterodine (1 systematic review and 1 RCT).

Compared with placebo, all antimuscarinics significantly improved LUTS and overall findings indicate that antimuscarinics are effective in improving overactive bladder symptoms in men.

The identified evidence is unlikely to change the guideline recommendation which states that men should be offered an antimuscarinic to manage the symptoms of overactive bladder.

One topic expert commented that there is insufficient warning about the potential for cognitive decline with antimuscarinic drugs. NICE produced the following document (we will include the following cross-referral on risk of the potential

cognitive decline with antimuscarinic drugs):

[‘Drugs with antimuscarinic effects and risk of cognitive impairment, falls and all-cause mortality’](#) which reviewed a systematic review and meta-analysis, of mostly observational studies, that reported that drugs with antimuscarinic effects were associated with an increased risk of cognitive impairment and all-cause mortality in older people, and some drugs were linked to an increased risk of falls. It concluded:

“Of late there has been a lot of interest in the potential harm caused by drugs that have antimuscarinic effects. Concerns exist that several treatments with some antimuscarinic activity might have cumulative harmful effects when given to a person with more than one clinical condition. This potential for harm increases with frailty and age. Various antimuscarinic burden or risk scales have been devised to aid medication reviews so that certain drugs can either be stopped, or the medication regimen altered to reduce this burden.

“This systematic review and meta-analysis by [Ruxton and colleagues](#) examines the evidence of cognitive impairment, falls and mortality from drugs with antimuscarinic effects. The evidence is not very strong, but there does appear to be an association between some individual drugs and these harms. There also seems to be a correlation between overall antimuscarinic burden and mortality.”

“Antimuscarinic risk scales are currently contained in various toolkits for

polypharmacy, such as those by NHS Scotland and the All Wales Medicines Strategy Group. The findings of the [Ruxton et al.](#) study provide reasonable support to continue using these tools when deciding on and reviewing treatments for older or frail people, or people with complex multi-morbidities.”

Phosphodiesterase 5 inhibitor (PDE5Is)

The evidence from 4 RCTs, 1 meta-analysis, and 2 post-hoc analyses in the 2014 review suggested that PDE5Is (tadalafil in particular) may be effective treatments for LUTS in men. New evidence in current review from a Cochrane systematic review also indicates that PDE5Is may significantly improve LUTS. However, the authors indicated that evidence was mostly limited to short-term treatment (up to 12 weeks) with moderate or low certainty. Current evidence from 1 systematic review, 1 meta-analysis and 6 RCTs suggests that tadalafil may improve nocturnal voiding frequency however, it appears to be less effective in older men.

This section was updated in 2015 and the evidence appeared that PDE5 inhibitors may not be clinical and cost effective in treatments of LUTS and BPH. New recommendation was added subsequently: ‘Do not offer phosphodiesterase-5-inhibitors solely for the purpose of treating lower urinary tract symptoms in men, except as part of a randomised controlled trial (1.4.10).

Tadalafil for benign prostatic hyperplasia is also covered in a product produced by the Evidence Summaries: New Medicines (ESNM) programme of the Medicines and

Prescribing Centre (MPC) at NICE: ESNM18 [Lower urinary tract symptoms secondary to benign prostatic hyperplasia: tadalafil](#) (Oct 2013).

All drugs

Findings from 1 systematic review that compared the efficacy of different treatments for improving LUTS showed that alpha blockers and 5-alpha reductase inhibitors (5-ARIs) improved bladder outlet obstruction index and maximum urinary flow rate. PDE5Is and phytotherapeutic compounds had no great effects on urodynamic parameters. Evidence from 1 RCT indicated that alfuzosin and tamsulosin had same efficacy in improving LUTS. This is in line with the current recommendations that recommend 5-ARIs and alpha blockers including alfuzosin and doxazosin for treatment of moderate to severe LUTS.

Desmopressin

The 2012 identified an RCT which reported that low dose desmopressin is an effective and safe treatment for nocturia in men aged ≥ 65 years with BPH.

The 2014 review identified 2 RCTs which found desmopressin significantly decreased nightly voids in men with BPH. A further RCT identified in 2014 review reported improvements in quality of life following desmopressin treatment.

New evidence from a Cochrane systematic review and an RCTs in current review indicates that desmopressin may reduce the number of nocturnal voids compared with placebo in intermediate-term (three

to 12 months) follow-up without increase in major adverse events.

The identified new evidence supports the guideline recommendation that oral desmopressin should be offered to men with nocturnal polyuria if other medical causes have been excluded and they have not benefited from other treatments.

Non-steroidal anti-inflammatory drugs (NSAIDs)

Evidence from a systematic review at 2014 review suggest that NSAIDs may improve urinary symptom scores and flow measures. No new evidence was identified in the current review.

This is in line with the evidence within the guideline. This evidence adds to the research recommendation on the clinical and cost effectiveness of NSAIDs compared with placebo in reducing symptom progression for men with lower urinary tract symptoms; further evidence is required on costs and long-term safety and efficacy.

Beta 3-adrenoceptor agonist

Evidence from previous review from 5 RCTs, 1 systematic review and pooled data from 3 RCTs suggested that mirabegron may improve LUTS better than a placebo. No new evidence was identified at the current review.

Evidence from the 2014 review from an RCT suggests that mirabegron and tolterodine may equally be effective improving overactive bladder symptoms.

Mirabegron is not included in the guideline but is covered in a related Technology

Appraisal: TA290 Overactive bladder – mirabegron (published June 2013): [Mirabegron for treating symptoms of overactive bladder](#).

Selective serotonin and norepinephrine reuptake inhibitor (SNRI) antidepressants

Duloxetine is not included in CG97. Evidence from 2014 review reported that incontinence and quality of life was improved with duloxetine but was insufficient to consider duloxetine for inclusion in the guideline. No new evidence was identified in the current review.

Nitrate

Isosorbide dinitrate is not included in CG97. Evidence from 2014 review from one RCT suggested effectiveness of sublingual isosorbide dinitrate for treating acute urinary retention but was insufficient for including isosorbide dinitrate in the guideline. No new evidence was identified at the current review.

Combination therapy

Alpha blockers plus 5-alpha reductase inhibitors (5-ARI) versus alpha blockers or 5-ARI

Evidence from 2012 and 2014 reviews indicated that following combinations therapy are more effective in improving LUTS compared with monotherapy:

Tamsulosin and dutasteride combination: 1 RCT

General (alpha blockers plus 5-alpha reductase inhibitors versus alpha blocker monotherapy with): 2 studies

New evidence from current review indicates that following combinations are more effective compared with onotherapy for LUTS secondary to BPH:

Tamsulosin and dutasteride combination: 1 RCT

Combination therapy reduced IPSS score at month 24, improved peak urinary flow at every assessment and reduced prostate volume at months 12 and 24 better than the monotherapy.

Tamsulosin plus finasteride versus Tamsulosin: 2 RCTs

Tamsulosin monotherapy and combination therapy appeared to be equally effective in improving IPSS score and peak urinary flow rate in one study and in the other study combination therapy significantly improved the total American Urological Association symptom score and residual urine volume compared with monotherapy.

Tamsulosin and finasteride plus omega-3 fatty acids versus tamsulosin and finasteride: 1 systematic review

Omega-3 fatty acids plus tamsulosin and finasteride showed higher improvement in IPSS, and Q max, at the 1, 3 and 6-month interval

Tamsulosin and dutasteride vs dutasteride: 1 systematic review

Combination therapy with dutasteride and tamsulosin resulted in significantly greater improvements in IPSS and Q max compared with tamsulosin monotherapy

General (alpha blockers plus 5-alpha reductase inhibitors versus alpha blocker monotherapy with): 1 study

Combination therapy with alpha blockers and 5-ARIs was associated with higher risk of ED compared with monotherapy

A combination of an alpha blocker and a 5-alpha reductase inhibitor is recommended in the current guideline for men with bothersome moderate to severe LUTS. New evidence on alpha blockers combination therapy is in line with the current recommendations and no new evidence was identified which would change the recommendation.

Alpha blockers plus PDE5Is versus Alpha blockers or PDE5Is

Evidence from 2014 review indicated that following combinations therapy are more effective in LUTS compared with monotherapy:

Doxazosin and sildenafil versus sildenafil: 1 RCT

Tamsulosin and vardenafil versus tamsulosin: 1 RCT

Tamsulosin and vardenafil versus tamsulosin: 5 studies (4RCTs and 2 post-hoc analyses)

Tamsulosin and tadalafil versus tamsulosin: 2 RCTs

Doxazosin and sildenafil versus sildenafil: 1 RCT

PDE5Is and alpha blockers versus PDE5Is or alpha blocker monotherapy: 1 systematic review

Evidence from 2014 review on following combinations reported that the combination therapy did not have a better efficacy than placebo or monotherapy

Alpha blockers and tadalafil versus placebo: 1 RCT

Alfuzosin and sildenafil versus alfuzosin: 1 RCT

New Evidence from current review indicates that following combinations therapy compared with monotherapy has a beneficial effect in treating men with LUTS secondary to BPH:

Tamsulosin and sildenafil versus tamsulosin: 1 RCT

Combination therapy did not improve urinary retention more than tamsulosin alone

Tamsulosin plus Xipayimaizipizi versus tamsulosin: 1 RCT

At 4 weeks, the combination group showed more improvement than the monotherapy group in nocturnal urination frequency, IPSS and maximum urine flow rate, and QoL.

Tamsulosin and tadalafil versus tamsulosin: 1 RCT

Combination treatment significantly improved IPSS, international index of erectile function questionnaire scores and maximum urine flow rate compared

Tamsulosin and tadalafil versus tamsulosin or tadalafil alone: 1 RCT

Tamsulosin and tadalafil, either alone or in combination, equally improved LUTS

Tamsulosin and solifenacin and versus placebo or tamsulosin: 1 RCT, 1 meta-analysis

Alfuzosin and tadalafil versus each monotherapy: 1 RCT

Compared with monotherapy, combination therapy significantly improved IPSS scores and post-void residual urine volume

Tamsulosin and sildenafil versus tamsulosin: 1 RCT

Sildenafil citrate plus tamsulosin improved LUTS, erectile function, and patient QoL more than tamsulosin.

General (alpha blockers and phosphodiesterase 5 inhibitors used alone or combined): 3 systematic reviews

Findings from 2 systematic reviews indicated that combination therapy greatly improved IPSS, maximum urine flow rate in patients with LUTS/BPH. The other systematic review reported that combination and monotherapy were equally effective in improving LUTS/BPH.

Tamsulosin and desmopressin versus tamsulosin: 1 RCT, 1 systematic review

Combined Alpha blockers and desmopressin lead to a decrease in the frequency of night voids.

Tamsulosin and ketoconazole versus tamsulosin: 1 RCT

The incidence of the successful trial without catheter was higher in the combined treatment group compared with the tamsulosin group.

Doxazosin plus Longbishu Capsule (LBS): 1 RCT

After 12-month treatment, groups showed improvements in IPSS and maximum urinary flow rate from baseline

General

In addition, evidence from 4 systematic reviews that evaluated the efficacy of alpha blockers with or without PDE5 inhibitors in patients with LUTS/BPH concluded that combination therapy may greatly improve IPSS, maximum urine flow rate, and sexual function in patients with LUTS/BPH.

A combination of an alpha blocker and a PDE5 inhibitor is not recommended in the current guideline for treatment of LUTS. The relevant evidence was updated in 2015 and it appeared that PDE5 inhibitors monotherapy and combination therapy may not be clinical and cost effective in treatments of LUTS and BPH. New recommendation was added subsequently: 'Do not offer phosphodiesterase-5-inhibitors solely for the purpose of treating lower urinary tract symptoms in men, except as part of a randomised controlled trial (1.4.10).

PDE5 inhibitor plus 5-alpha reductase inhibitor (5-ARI)

Evidence from an RCT at 2014 review suggests that co-administration of tadalafil/finasteride may provide early LUTS improvement in men with BPH and prostatic enlargement. New evidence in current review from 2 RCT supports the efficacy of tadalafil co-administered with finasteride for improving LUTS.

The guideline does not include recommendations on the use of PDE5

inhibitors and 5-alpha reductase inhibitor combination therapy for LUTS and currently there is insufficient new evidence on long-term efficacy of the combination to enable a recommendation to be made.

Antimuscarinic plus alpha blockers

The 2012 Evidence update identified an RCT which indicated that the combination group (alpha blockers plus antimuscarinic) had significantly improved urinary symptoms compared with monotherapy.

Evidence from 2014 review supports the efficacy and safety of following antimuscarinics combination with alpha blockers in treating men with LUTS:

Trospium chloride and terazosin versus terazosin and placebo: 1 RCT

Propiverine and terazosine versus terazosine and placebo: 1 RCT

Tolterodine and alpha blockers and/or 5-alpha reductase inhibitors versus tolterodine: 1 RCT

Imidafenacin and tamsulosin versus tamsulosin: 3 systematic review, 2 RCTs

Solifenacin and tamsulosin versus placebo or tamsulosin: 5 RCTs

Fesoterodine and tamsulosin versus tamsulosin: 2 RCTs

Tolterodine and tamsulosin versus tolterodine or tamsulosin: 1 RCT

New evidence from current review indicates that following combinations therapy compared with monotherapy may improve LUTS in particular storage urinary

symptoms and overactive bladder in men with BPH:

Propiverine plus silodosin versus silodosin: 1 RCT

Antimuscarinics and alpha blockers versus to alpha blocker monotherapy: 1 Cochrane review, 1 meta-analysis, 2 RCTs (one RCT on men previously treated and unresponsive to an alpha blocker)

Solifenacin and tamsulosin and versus tamsulosin: 5 RCTs

Imidafenacin and tamsulosin and dutasteride (5-ARI) versus tamsulosin and dutasteride: 1 RCT

Imidafenacin and tamsulosin and dutasteride (5-ARI) versus tamsulosin and dutasteride monotherapy: 1 RCT

Imidafenacin and dutasteride (5-ARI) and versus tamsulosin: 1 RCT

Tamsulosin and Solifenacin and versus tamsulosin: 1 RCT

solifenacin and mirabegron vs solifenacin: 1 meta-analysis, 1 RCT

Propiverine and alfuzosin versus alfuzosin: 1 RCT

Tolterodine extended release (ER) plus tamsulosin versus ER monotherapy: 1 RCT

The guideline recommends that men should be offered an antimuscarinic as well as an alpha blocker if they still have storage symptoms after treatment with an alpha blocker alone. From the assessment of abstracts, it was not always clear whether men had previously received alpha blocker treatment. The findings were mixed with some reporting a benefit of

combination therapy for some outcomes whereas others did not observe a difference between monotherapy and combination therapy. As such, there is currently insufficient conclusive new evidence which would impact on the guideline recommendation.

NSAID (non-steroidal anti-inflammatory drugs) plus alpha blockers

Evidence from an RCT at 2014 review suggests that combination therapy of celecoxib plus terazosin may improve LUTS better than the terazosin monotherapy. New evidence from an RCT in current review supports the use of tamsulosin hydrochloride plus meloxicam for improving urinary flow rates.

The guideline does not include recommendations on the use of alpha blocker and NSAID combination therapy and currently there is insufficient new evidence to enable a recommendation to be made.

Beta 3-adrenoceptor agonist combination therapy

No evidence was identified at the previous review. New evidence from current review supports efficacy of following combination in improving LUTS in men with BPH.

Mirabegron plus tamsulosin versus tamsulosin - 1 RCT

Mirabegron plus solifenacin versus solifenacin - 1 RCT

Vibegron and tolterodine versus vibegron or placebo - 1 RCT

Mirabegron is not included in the guideline but is covered in a related Technology

Appraisal: TA290 Overactive bladder – mirabegron (published June 2013): [Mirabegron for treating symptoms of overactive bladder](#).

The guideline does not include recommendations on the use of beta 3-adrenoceptor agonist combination therapy

for BPH and currently there is insufficient new evidence to enable a recommendation to be made.

New evidence is unlikely to change guideline recommendations.

1.5 Surgery for voiding symptoms

Recommendations in this section of the guideline

- 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.
- 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.
- 1.5.3 Offer transurethral incision of the prostate (TUIP) as an alternative to other types of surgery (see 1.5.2) to men with a prostate estimated to be smaller than 30 g.
- 1.5.4 Only offer open prostatectomy as an alternative to TURP, TUVP or HoLEP (see 1.5.2) to men with prostates estimated to be larger than 80 g.
- 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 1.5.2).
- 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.
- 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.

Surveillance proposal

This section of the guideline should be updated.

Surgery for voiding symptoms

Transurethral resection of the prostate (TURP)

TURP versus Photoselective vaporisation of the prostate (PVP)

Previous surveillance summary

Overall findings from 2 systematic reviews (206,207), 2 metaanalysis (208,209) and 5 RCTs (including 1 noninferiority trial) and 1 cost effective analysis (210–215) identified in 2014 review indicated that photoselective vaporisation of prostate and TURP had similar efficacy and safety in treatment of LUTS caused by BPH. The noninferiority trial (212) on photoselective vaporisation of the prostate compared with TURP showed that photoselective vaporisation was not as effective as TURP but showed that it was associated with a shorter length of stay in the hospital.

2019 surveillance summary

A systematic review (216) of 11 studies compared monopolar TURP and photoselective vaporisation of the prostate (PVP) for treatment of LUTS due to BPH. Compared with PVP, monopolar TURP reduced operative time but increased hospitalisation time. PVP reduced transfusion rate and clot retention but resulted in similar rates of acute urinary retention and urinary tract infection. The long-term complications of

bladder neck contracture and urethral stricture, IPSS and maximum urine flow rate were similar between PVP and monopolar TURP.

A systematic review of 4 studies (217) (total n=559) assessed the efficacy and the safety of Greenlight (TM) high-performance system (HPS) 120-W laser PVP compared TURP for treatment of BPH. There was no significant difference in IPSS and maximum urine flow rate between PVP and TURP at 6, 12, and 24-month follow-up. In the TURP group, there was a lower risk of re-operation (RR=3.68) and a shorter operative time (MD=9.28) than in the PVP group.

An RCT (218) compared photoselective vaporisation with the GreenLight 120-W Laser and monopolar TURP as surgical treatments of prostates <80cc in 101 men with obstructive BPH. Postoperative functional improvements were similar in the 2 groups in IPSS, Sexual Health Inventory for Men, maximum urine flow rate postmicturition residual parameters and postoperatively complication rates between the 2 groups.

An RCT (219) evaluated the efficacy of potassium titanyl phosphate (KTP) PVP laser versus TURP for the treatment of BPH with long-term follow-up period (48 months) in 150 men with BPH. IPSS score improved in both TURP and KTP groups from the baseline. There was improvement

in maximum urine flow rate during follow-up in both groups which was maintained at 48 months.

An RCT (220) compared the effectiveness and complications of 980-nm diode laser vaporisation and TURP in 72 patients with BPH. PVP with a diode laser had similar complication rates and functional results (maximum urine flow rate, IPSS and IPSS-QoL) at 3 months post operation. PVP had the advantage of shorter hospitalisation and catheter indwelling times.

An RCT (221) compared outcomes of diode laser vaporisation of prostate with TURP as a gold standard treatment. In the TURP group, the catheterisation time and postoperative hospital stay was significantly longer than in the diode group. The 2 treatments similarly improved maximum urine flow rate, IPSS, and post-void residual urine volume during the first 6 months. However, at 12 and 24 months of follow-up the TURP improved IPSS and maximum urine flow rate more than the diode treatment.

An RCT (223) assessed the long-term functional and safety of 80-W GreenLight photoselective vaporisation (GL PV) of the prostate and TURP in 105 men. After 5 years of treatment, mean improvements in IPSS, postvoidal residual and maximum urinary flow rate were similar in both groups. The re-treatment rate was 14.3% in the GL PV group vs 11.9% in the TURP group.

An RCT (224) comparing the safety and efficacy of bipolar TURP and PVP in 78 patients under sedoanalgesia. PVP patients had a shorter operating time (mean 55.64

vs 61.79 min), shorter duration of hospitalisation (mean 14.58 vs 19.21) and a higher dysuria rate when compared to biolar TURP patients. Improvements in IPSS, quality of life, prostate volume, Qmax and post-void residual urine volume at 3 months were similar in both groups.

Bipolar versus monopolar TURP

Previous surveillance summary

An RCT ([Fagerstrom et al. 2011](#)) identified in the 2012 Evidence update found patients treated with bipolar TURP had fewer readmissions compared with those treated with the monopolar TURP.

However, finding from a systematic review(225) showed that the 2 treatment modalities did not differ significantly with respect to operation times, transfusion rates, retention rates after catheter removal and urethral complications although there was a suggestion that bipolar TURP may reduce bleeding and complications.

Evidence from 8 RCTs (222,226–232) identified in the 2014 review reported that monopolar and bipolar TURP both improved LUTS symptoms with no significant differences between the interventions.

2019 surveillance summary

An RCT (233) analysed the incidence of stricture urethra among patients undergoing mono polar TURP versus bipolar TURP in 40 men with BPH. The incidence of stricture urethra following bipolar TURP was comparable to the conventional monopolar TURP at 3, 6 and 12 months follow-up.

A systematic review (234) of 31 studies evaluated the efficacy and safety of monopolar TURP and bipolar TURP in men with benign BPH. Bipolar TURP was associated with a lower rate of clinically relevant complications (such as blood clot retention) compared with monopolar TURP. Blood transfusion frequency or late complications were similar in both groups.

An RCT (235) compared monopolar versus bipolar TURP in 137 patients with BPH. The two groups were similar postoperatively in duration of surgery, catheterisation, hospitalisation, blood loss, rates of blood transfusion, IPSS, IPSS-QoL scores, rates of rehospitalisation, clot retention, blood transfusions, and re-operation or urethral strictures. However, bladder neck stricture occurred more often in the bipolar group (8.5% vs 0%). Micturition improved equally in the two groups at 3 and 12-month follow-up.

An RCT (236) evaluated the safety and efficacy bipolar transurethral plasma vaporisation (B-TUVP group I) with monopolar TURP (group II) for the treatment of BPH in 82 men. The remote postoperative complication rate was 15% in group I and stress urinary incontinence 5%, bladder outlet obstruction 5%, and residual adenoma 5%. In group II, the remote postoperative complication rate was 4.8%. There were improvements in micturition variables postoperatively in both arms, but the magnitude of improvement was greater in group II. There was similar efficacy in IPSS, PVR, and maximum urine flow rate in two groups.

An RCT (237) compared the efficacy and safety and complication rates of monopolar versus bipolar TURP in 81 men with prostate volume >60 mL. Bipolar and monopolar TURP showed similar effect and safety. Serum sodium level increased more in monopolar TURP post operation compared with bipolar TURP.

TURP versus thulium laser vaporesection/resection of the prostate

Previous surveillance summary

No evidence was identified in the 2012 Evidence update. Findings from an RCT (238) identified in the 2014 review comparing thulium laser vaporesection of the prostate with TURP in men with BPH reported that acute complications, improvements in IPSS and maximum urinary flow rates, were similar in both groups. Another study (239) identified in the 2014 review which compared the efficacy and safety profile of bipolar hybrid prostate surgery (using both resection and vaporisation modes) with bipolar resection undertaken in men with BPH reported that hybrid group had a significantly shorter postoperative catheter time.

2019 surveillance summary

A systematic review (240) of five studies compared efficacy and safety of bipolar TURP and Thulium laser vaporisation (ThuVAP) and for the treatment of BPH. ThuVAP and bipolar TURP both improved IPSS, QoL, PVR, and maximum urine flow rate. ThuVAP resulted in less blood loss as well as shorter hospitalisation and catheterisation time but required longer surgical time.

A systematic review (241) of 9 studies assessed the efficacy and safety of thulium laser resection of the prostate (TmLRP) compared with TURP for treating patients with BPH. Compared with TURP, although TmLRP needed a longer operative time, patients having TmLRP had significantly less serum sodium decreased, less serum haemoglobin decreased, shorter time of catheterisation, shorter length of hospital stay, and fewer total complications (OR=0.29). During the 1, 3, 6, and 12 months of postoperative follow-up, the two groups were comparable in terms of peak urinary flow rate, IPSS, post-void residual rate, and quality of life.

An RCT (242) compared the efficacy of thulium laser resection of the prostate-tangerine technique (TmLRP-TT) with TURP for treatment of LUTS in 96 men with BPH at 12, 24, 36, and 48 months postoperatively. All micturition parameters in the TmLRP-TT group were similar to those of TURP patients at every annual assessment. Re-operation rates were equal in the two groups.

An RCT (243) compared early postoperative outcomes between thulium laser transurethral enucleation of the prostate (ThuLEP) and transurethral bipolar resection in saline (TURiS) in 208 men with BPH. Compared with TURiS, ThuLEP had same operative time but reduced haemoglobin decline. ThuLEP also needed less catheterisation time and hospital stay. During the 3 months of follow-up, the procedures were similar in maximum urine flow rate, IPSS, PVR, and QoL.

An RCT (244) compared the safety and efficacy of thulium laser enucleation of the prostate (ThuLEP) versus thulium laser resection of the prostate (TmLRP) in 115 men with BPH and small prostates (≤ 30 g). The postoperative improvement among the groups in the IPSS, quality of life, maximal urinary flow rate and PVR were similar at the 12-month follow-up.

TURP versus transurethral resection and holmium laser enucleation (HoLEP)

Previous surveillance summary

The 2012 Evidence update identified one RCT ([Eltabey et al. 2010](#)) that found HoLEP and bipolar TURP were equally effective in treating patients with LUTS due to BPH.

Evidence from 2014 review from 3 RCTs (245–247) showed that both surgical treatments were equivalent in improving lower urinary tract symptoms.

A systematic review (248) and RCT (249) identified in the 2014 review comparing TURP with HoLEP for BPH found that both interventions improved IPSS and maximum urine flow rate. The review reported that the maximum urine flow rate and IPSS in the HoLEP group were significantly better than those in the TURP group at 12 months postoperatively while the RCT found that patients in the HoLEP group needed shorter times with catheters and shorter hospital stays. Conversely, a meta-analysis (250) comparing the efficacy and safety of TURP with HoLEP found the highest reduction of the IPSS in the TURP group.

2019 surveillance summary

A systematic review (251) of 4 studies assessed the efficacy and safety of bipolar TURP versus HoLEP for the treatment of BPH. The two treatments were comparable in terms of peak urinary flow rate, IPSS, post-void residual volume at 3-6 months follow-up, operation duration, catheterisation duration, resected tissue and complications. HoLEP was associated with a significantly shorter irrigation time as compared with bipolar TURP.

A meta-analysis (252) of 15 studies (n=855) assessed the efficacy of HoLEP compared with TURP in patients with BPH. There was no significant difference in quality of life between the two treatment groups, but peak urinary flow rate at 3 months and 12 months, PVR at 6, 12 months, and IPSS at 12 months were improved better in HoLEP treatment group compared with TURP treatment group. There was no significant difference in early and late postoperative complications, and HoLEP was associated with longer operation time (WMD 14.19) shorter catheterisation time (mean difference -19.97) and shorter hospital stay (mean difference -25.25 h).

An RCT (253) evaluated long- and short-term outcomes of HoLEP in 144 men with BPH and prostate >60 g. HoLEP was associated with less blood loss, lower transfusion rates, and a shorter hospital stay but longer operative time and more postoperative dysuria.

An RCT (254) evaluated the efficacy and safety of HoLEP and TURP, for treatment of 164 men with BPH. The two groups had

comparable operation time, catheterisation time, and length of hospital stay. However, HoLEP treatment was significantly better in terms of weight of resected prostate tissue, bladder irrigation time, haemoglobin levels and blood sodium levels after surgery. The two groups were comparable in the peak urinary flow rate, post-void residual volume, IPSS, or quality of life score at 1 month after surgery. But after 12 months, patients from the HoLEP group demonstrated better scores in peak urinary flow rate, post-void residual volume, IPSS, and quality of life than those from the TURP group.

C-TURP (channel TURP) combined with interstitial laser coagulation

Previous surveillance summary

The 2014 review identified an RCT (255) that assessed the clinical effectiveness of channel transurethral resection of the prostate (C-TURP) combined with an interstitial laser coagulation (ILC) technique in men with BPH. C-TURP plus ILC appeared safe and effective for the treatment of BPH and exhibited favourable short-term clinical response and long-term durability.

2019 surveillance summary

No relevant evidence was identified.

TURP versus transurethral plasma kinetic enucleation of the prostate (TPKEP)

Previous surveillance summary

The 2014 review identified an RCT (256) compared the perioperative and postoperative characteristics of prostate Plasma Kinetic enucleation and bipolar TURP for large volume BPH. The

postoperative improvement in IPSS, QoL, maximal flow rate and post-void residual urine volume was similar in both groups at 1, 6, 12 and 24 months but significantly better in the enucleation group at 36, 48 and 60 months.

2019 surveillance summary

An RCT (257) evaluated the efficacy and safety of transurethral plasma kinetic enucleation of the prostate (TPKEP) and TURP in 80 men with BPH. TPKEP group was superior to the TURP group in in blood loss, duration of operation, time of bladder irrigation, duration of indwelling catheter, postoperative irritation sign of the bladder and urethra, and the event of indwelling catheter after removal.

However, the incidence of transient uracratia was higher in TPKEP group than the TURP group. IPSS, maximum urine flow rate and PVR were equally improved in both groups at 6-month follow-up.

An RCT (258) evaluated the efficacy of electrosurgical enucleation versus bipolar TURP for treatment of LUTS in 80 men with prostates volume >70 ml.

PlasmaKinetic enucleation of the prostate was associated with less blood loss, shorter hospital stay and catheterisation time than bipolar TURP.

TURP versus Transurethral enucleation of the prostate (TUERP)

Previous surveillance summary

No evidence was identified at the 2012 Evidence update. The 2014 review identified an RCT(260) which compared the clinical outcomes between thulium laser transurethral enucleation of the

prostate and plasmakinetic bipolar resection of the prostate for treating BPH. The results indicated that both interventions relieved LUTS equally, with high efficacy and safety.

2019 surveillance summary

An RCT (261) compared the efficacy and safety of TURP and TUERP for treatment of BPH in 630 men. TUERP appeared better than TURP with higher resection rate of the prostate, shorter operation time and bladder irrigation time, less intraoperative blood loss, fewer postoperative complications, and faster recovery.

TURP versus 'button type' bipolar plasma vaporisation (BTPV)

Previous surveillance summary

An RCT (214) reported the superiority of bipolar plasma vaporisation of the prostate with 'button type' electrode over standard TURP for improving LUTS. One study (215) from a non-UK setting reported that photoselective vaporisation was less costly compared with TURP.

2019 surveillance summary

A systematic review and metanalysis (262) of 6 RCTs (total n=871) evaluated the efficacy of 'button type' bipolar plasma vaporisation (BTPV) in improving symptoms of BPH compared with TURP (monopolar or bipolar). The improvement of urinary symptoms and overall complications in BTPV were comparable with conventional TURP. The number of complications following the surgery was similar between the groups. However, there was a tendency for a higher

transfusion rate in the TURP group. The average duration of indwelling catheterisation was less in patients who underwent BTPV. Overall, both treatments improved symptoms and the postoperative IPSS was similar in two groups.

TURP versus transurethral incision of the bladder neck

Previous surveillance summary

An RCT (259) was identified in 2014 review that assessed safety and efficacy of selective transurethral resection of the prostate (STURP) in combination with transurethral incision of the bladder neck (TUIBN) compared with TURP for BPH. At 6 months postoperatively, no significant difference in IPSS was observed between the two groups although the maximum urine flow rate in patients receiving STRUP+TUIBN was markedly higher than in those receiving TURP.

2019 surveillance summary

No relevant evidence was identified.

TURP versus prostatic artery embolisation (PAE)

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance summary

A systematic review (263) of 4 studies (total n=506) evaluated the clinical efficiency and safety of TURP and prostatic artery embolisation (PAE) for treatment of BPH. TURP significantly improved maximum urine flow rate and QoL and decreased prostate volume compared with PAE. postoperative IPSS

and complications were similar in two groups.

A systematic review (264) of 4 studies evaluated the clinical outcomes and peri-operative complications of PAE in patients treated for LUTS related to benign prostatic obstruction. When compared to TURP, PAE was associated with a lower IPSS reduction at 1 and 3 months after the procedure. A trend toward similar symptoms improvement was however reported from 6 to 24 months.

An RCT (265) evaluated the PAE and TURP in 114 men with BPH. Success rates for TURP and PAE were 100% and 94.7%, respectively; the clinical failure rates were 3.9% and 9.4%, respectively. However, the TURP group showed greater degrees of improvement in IPSS, QoL, peak urinary flow, and post-voiding residual urine volume at 1 and 3 months, as well as greater reductions in the PSA level and prostate volume at all follow-up time points, when compared with the PAE group. The PAE group showed more overall adverse events and complications, mostly related to acute urinary retention (25.9%), postembolisation syndrome (11.1%), and treatment failures (5.3% technical; 9.4% clinical).

TURB versus transurethral resection in saline (TURis)

Previous surveillance summary

No relevance evidence was identified.

2019 surveillance summary

A systematic review (266) of 11 RCTs evaluated the efficacy of bipolar transurethral resection in saline (TURis) as

an alternative surgical option to monopolar TURP. The TURis system was associated with better improvements in perioperative safety and reduced hospital stay compared with monopolar TURP.

An RCT (267) evaluated the safety and efficacy of transurethral resection in saline (TURis) bipolar vaporisation of the prostate relative to monopolar TURP in 84 men with BPH. TURis bipolar vaporisation had a longer operative time than monopolar TURP. Postoperatively, the TURis group had a shorter catheter time and a shorter length of hospital stay. The postoperative dysuria score was higher in the TURis vaporisation arm. Quality of life score was similar in two groups at 3 and 6 months.

TRUP versus transurethral vaporisation of the prostate (TUVP)

Previous surveillance summary

No evidence was identified at the 2012 Evidence update. Findings from an RCT (268) identified at 2014 review did not report any significant differences on safety and effectiveness of transurethral vaporisation of the prostate (TUVP) compared with standard TURP in treatment of BPH.

2019 surveillance summary

A systematic review (269) of 7 RCTs (total n=1,071) assessed the efficacy and safety of bipolar plasma vaporisation of the prostate (BPVP) in the management of bladder outlet obstruction due to BPH. Compared with TURP, BPVP had superior haemostatic efficiency and shorter catheterisation time (42.5 versus 77.5 hours), shorter hospital stay (3.1 versus 4.4

days) and slightly better short-term functional outcomes.

An RCT (270) compared the outcomes of bipolar transurethral vaporisation of the prostate (TUVP) with bipolar TURP in 88 men with moderate to severe LUTS and prostate volume of 30 to 80 mL. The TUVP group had significantly lower mean values of operative time, hospital stay, catheterisation period, irrigation fluid volume and serum haemoglobin, compared with TURP group. Postoperative complications were similar in two groups. Three months after surgery, TUVP improved IPSS and maximum urine flow rate better than the TURP group.

TURP versus GreenLight XPS Laser (GLP-XLS)

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance summary

An RCT (271) examined whether treatment effects observed at 6 months between GreenLight XPS (GL-XPS) and TURP was maintained at the 2-year follow-up in 160 men with BPH. The long-term effectiveness and safety of GLP-XLS on IPSS, maximum urine flow rate, PSA, prostate volume, and overactive bladder was comparable to conventional TURP for the treatment of LUTS.

C-BPVP, S-BPVP, M-TURP

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance summary

An RCT (272) investigated efficiency and safety of three surgery methods: continuous bipolar plasma vaporisation of the prostate (C-BPVP), standard vaporisation (S-BPVP) and monopolar TURP for improving LUTS in 180 men with BPH. C-BPVP and S-BPVP had better perioperative safety and improved follow-up voiding and symptom scores than TURP.

TURP compared with medications

Previous surveillance summary

No evidence was identified at the 2012 Evidence update. The 2014 review identified an RCT(273) which compared the effect of tamsulosin versus TURP for the management of nocturia in previously untreated men with LUTS and BPH. Both interventions improved study outcomes although TURP was associated with a significant improvement in the number of nocturnal awakenings and quality of life in comparison with tamsulosin.

Previous surveillance summary

No relevant evidence was identified.

Holmium laser enucleation of the prostate (HoLEP)

Previous surveillance summary

Evidence from 2014 review from 1 RCT (274) reported higher maximum flow rate and lower post-void residual urine in holmium laser cases during follow-up.

2019 surveillance summary

No relevant evidence was identified.

Holmium laser versus conventional monopolar electrocautery (C-BNI)

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance summary

An RCT (275) compared the efficacy and results of bladder neck incision (BNI) in 140 men with BPH and small prostate (≤ 30 cc) using holmium laser versus conventional monopolar electrocautery technique. The incidence of postoperative haematuria and blood transfusion in the C-BNI group were 4.2% and 2.8%, respectively. No patient in the holmium laser group developed haematuria or required blood transfusion. Maximum urine flow rate, and post-void residual at 6 months were similar in two groups. At 6 months, 2.9% patients in the holmium group and 4.3% in the C-BNI group remained obstructed urodynamically and underwent re-operation.

HoLEP versus plasma kinetic enucleation and resection of the prostate

Previous surveillance summary

No evidence was identified in the 2012 Evidence update. The 2014 review identified a trial (276) that indicated the laser enucleation of the prostate had significantly shorter operative time, postoperative irrigation time and catheterisation time compared with plasma kinetic enucleation and resection of the prostate in men with bladder outflow obstruction.

2019 surveillance summary

No relevant evidence was identified.

HoLEP versus thulium laser transurethral enucleation of the prostate

Previous surveillance summary

No evidence was identified at the 2012 review. One RCT (277) was identified at 2014 review that compared thulium laser transurethral enucleation of the prostate with HoLEP in men with BPH. At 18 months, the lower urinary tract symptom indexes were improved significantly in both groups compared with the baseline values.

2019 surveillance summary

An RCT (278) compared the perioperative outcomes of thulium vapoenucleation of the prostate (ThuVEP) with HoLEP for patients with BPH. There were no significant differences between the groups regarding, operation time, catheterisation time and postoperative hospital stay and surgical complications. However, the occurrence of acute postoperative urinary retention was higher after HoLEP compared to ThuVEP (15.2 versus 2.1%). At 1-month follow-up, peak urinary flow rates, post-void residual volumes, IPSS, QoL had improved significantly from baseline without significant differences between the groups.

An RCT (279) compared the perioperative and postoperative characteristics of thulium vapoenucleation and holmium laser enucleation of the prostate for the treatment of large volume prostate (median 80 cc) in 94 men. There were no significant differences between the groups regarding median operative time, catheter time, postoperative complications and median PSA at 6-month follow-up.

HoLEP versus Laser photoselective vaporisation of the prostate

Previous surveillance summary

The 2012 evidence identified an RCT ([Capitan et al. 2011](#)) that found no differences in laser vaporisation and TURP in IPSS reductions or maximum urine flow rate in men with LUTS and BPH. A cost effectiveness study based on the UK healthcare setting (Armstrong et al. 2009) at 2012 Evidence update concluded that initial ablation with diathermy vaporisation, followed by HoLEP for treatment failures, had an 85% probability of being cost effective at £20,000 per quality adjusted life year.

One RCT (280) was identified at the 2014 review which found that photoselective vaporisation of the prostate was equally effective and safe as holmium laser ablation of the prostate in men with BPH. In addition, the results of an RCT (281) indicated that high-power photovaporisation of the prostate can achieve and maintain the same results as TURP over a period of 24 months for LUTS caused by BPH.

2019 surveillance summary

No relevant evidence was identified.

HoLEP versus transurethral electrovaporisation resection of the prostate (TUEVP)

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance summary

An RCT (282) compared the safety and efficacy of the transurethral

electrovaporisation resection of the prostate (TUEVP) and holmium laser enucleation of the prostate (HoLEP) in treating BPH in 100 men. At 2 weeks and 3 months following the surgery the incidence of stress incontinence in HoLEP group were lower than those in TUEVP group, while there was no significant difference on the IPSS and maximum urine flow rate at 3-month follow-up.

Thulium laser resection

Thulium laser resection of the prostate-tangerine technique (TmLRP-TT) versus plasmakinetic resection of the prostate (PKRP)

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance summary

An RCT (283) compared the safety and efficacy of thulium laser resection of the prostate-tangerine technique (TmLRP-TT) and plasmakinetic resection of the prostate (PKRP) in 90 men with BPH and volume prostates >80 ml. Compared with the PKRP group, the TmLRP-TT group had a lower haemoglobin drop, shorter catheterisation time and hospital stay. Postoperative improvement in IPSS, QoL, maximum flow rate and PVR, was similar in two groups at 18-month follow-up.

Thulium laser enucleation of the prostate (ThuLEP) versus plasmakinetic enucleation of the prostate (PKEP)

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance summary

An RCT (284) compared the safety and efficacy of thulium laser enucleation of the prostate (ThuLEP) with plasma kinetic enucleation of the prostate (PKEP) in 127 men with BPH. The decrease in haemoglobin level and the catheter time were significantly lower in the ThuLEP group compared with the PKEP group. The 12-month follow-up showed no significant difference in urinary parameters between the two groups.

Thulium laser resection of prostate (ThuRP) versus plasmakinetic resection of the prostate (PKRP)

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance summary

A systematic review (285) of 9 studies compared the safety and efficacy of thulium laser resection of prostate (ThuRP) and PKRP for BPH. ThuRP was associated with longer operation time, shorter hospital stay, irrigation, and catheterisation duration. Estimated blood loss and drop in haemoglobin level were significantly more in PKRP. Except the quality of life score, which was better in ThuRP, the postoperative data (IPSS, maximum urine flow rate, post-void residual urine volume, severe bleeding, temporary urinary retention, temporary incontinence, urinary tract infection, urethral stricture) did not differ significantly.

Transurethral microwave thermotherapy

Previous surveillance summary

No evidence was identified in the 2012 Evidence update. The 2014 review identified a Cochrane systematic review (286) which assessed the therapeutic efficacy and safety of microwave thermotherapy techniques for treating men with symptomatic benign prostatic obstruction. The pooled mean urinary symptom scores decreased by 65% with transurethral microwave thermotherapy and by 77% with TURP.

2019 surveillance summary

No relevant evidence was identified.

Prostatectomy

Transvesical open prostatectomy versus plasma enucleation of the prostate

No evidence was identified in the 2012 Evidence update. Two RCTs (213,287) identified in the 2014 review comparing plasmakinetic enucleation of the prostate and transvesical open prostatectomy for BPH reported that both groups had a similar and significant postoperative improvement from baseline in quality of life and maximum urine flow rate, post-void residual (PVR) urine volume and prostate specific antigen.

Transvesical prostatectomy versus transurethral enucleation and resection of the prostate

Previous surveillance summary

No evidence was identified at the 2012 Evidence update. An RCT (288) identified in the 2014 review comparing the efficacy and safety of transurethral enucleation and

transvesical prostatectomy found that both interventions had similar efficacy for treatment of LUTS in men with BPH.

2019 surveillance summary

No relevant evidence was identified.

Bipolar transurethral plasmakinetic prostatectomy versus thulium laser resection of the prostate

Previous surveillance summary

No evidence was identified at the 2012 Evidence update. An RCT (289) was identified in the 2014 review that compared the safety and efficacy of thulium laser resection of the prostate and bipolar transurethral plasmakinetic prostatectomy in men with BPH. Similar and significant postoperative improvement in both groups in IPSS, QoL, maximum urine flow rate and PVR was reported at 3 months after the operation.

2019 surveillance summary

No relevant evidence was identified.

Open prostatectomy versus bipolar transurethral resection of the prostate

Previous surveillance summary

No evidence was identified at the 2012 Evidence update. The 2014 review identified an RCT (290) that assessed the efficacy and safety of bipolar TURP versus standard open prostatectomy in patients with LUTS due to bladder outlet obstruction. Data on IPSS symptom score, sexual function, and QoL, PSA, peak urinary flow rates and post-void residual urine volume were similar in two groups although postoperative catheterisation, hospital stay and 3-year overall surgical re-

treatment free rate were significantly better in the bipolar TURP group.

2019 surveillance summary

No relevant evidence was identified

Open prostatectomy versus holmium laser enucleation of the prostate (HoLEP)

Previous surveillance summary

No relevant evidence was identified

2019 surveillance summary

A systematic review (291) of 3 RCTS (N=263) evaluated the safety and efficacy of HoLEP and open prostatectomy (OP), robot-assisted, laparoscopic) for large prostate. The mean prostate volume was 113.9 mL in the HoLEP group and 119.4 mL in the OP group. There was no significant difference in peak urinary flow rate, post-void residual urine volume, IPSS and quality of life at 12 and 24 months between the two interventions. OP was associated with a significantly shorter operative time and greater tissue retrieved. However, HoLEP was associated with significantly less blood loss, shorter hospital stay, catheterisation time.

Transurethral enucleation and resection of the prostate (TUERP) and transvesical prostatectomy (TVP)

Previous surveillance summary

No relevant evidence was identified.

Previous surveillance summary

An RCT (292) evaluated the efficacy and safety of transurethral enucleation and resection of the prostate (TUERP) and transvesical prostatectomy (TVP) in 100 men with BPH and prostate volumes

>80 mL. Patients who underwent TUERP had shorter catheterisation times and hospital stays. Operation duration was similar between the two surgical groups. IPSS, PVR, maximum urine flow rate or QoL scores at 3 and 12 months and adverse events were also similar between the two groups.

2019 surveillance summary

No relevant evidence was identified.

laparoscopic simple prostatectomy (LSP) versus B-TURP

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance summary

An RCT (293) compared the efficacy of laparoscopic simple prostatectomy (LSP) with bipolar TURP in 90 men with BPH and prostate volume >80 mL. Compared with bipolar TURP, LSP was accompanied by less residual adenoma, shorter catheterisation time, and more blood loss. At 1, 3, 6, and 12 months post operation, improvement was similar in post-void residual urine volume, maximum urine flow rate, and IPSS in two groups. The improvement was in favour of LSP at 24 and 36 months following the surgery.

Thulium laser prostatectomy (TmLRP) versus TURP

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance summary

A systematic review (294) of 7 studies assessed the efficacy and safety of thulium laser versus TURP for treating patients

with benign prostatic obstruction. Compared with TURP, thulium laser prostatectomy (TmLRP) needed a longer operative time [weighted mean difference (WMD) 8.18 min], shorter time of catheterisation (WMD -1.29 days), shorter length of hospital stay (WMD -1.83 days), and less transfusion (odds ratio 0.09). During the 1, 3, and, 12 months of postoperative follow-up, the procedures did not show a significant difference in IPSS, QoL, maximum urine flow rate, and PVR.

Open prostatectomy versus plasmakinetic enucleation of the prostate (PKEP)

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance summary

An RCT (295) assessed the efficacy of plasmakinetic enucleation of the prostate (PKEP) compared with open prostatectomy in 153 men with large prostates (>100 gr). PKEP showed long-term micturition improvement equivalent to OP and lower perioperative morbidity.

Other laser treatments

Diode laser enucleation of the prostate (DiLEP) to Bipolar endoscopic enucleation of the prostate (BEEP)

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance review

An RCT (296) compared a modified diode laser enucleation of the prostate (DiLEP) to Bipolar endoscopic enucleation of the prostate (BEEP) in 114 patients with

prostate size of 20-160 mL. DiLEP was comparable to BEEP regarding maximum urine flow rate, and IPSS at 12 months. There were also no significant difference between two groups regarding, haemoglobin decrease, sodium decrease, and further need for surgery at 12 months.

Laparoscopic adenomectomy (LA) and Eraser laser enucleation of the prostate (ELEP)

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance review

An RCT (297) evaluated functional outcomes and morbidity rates after laparoscopic adenomectomy (LA) and Eraser laser enucleation of the prostate (ELEP) in 40 men with LUTS and prostate >70 g. Less blood loss, shorter catheterisation times, and shorter hospital stays was observed in the ELEP group. The two groups were comparable in IPSS scores and maximum urine flow rate throughout 3- and 6-months follow-up period.

Auriculotherapy (AT) using laser AT (LAT) and magneto-AT (MAT)

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance review

An RCT (298) examined whether a combined auriculotherapy (AT) using laser AT (LAT) and magneto-AT (MAT) is more effective than using MAT alone or placebo for managing LUTS in 40 men. A combined AT approach was associated with greater

improvements in relieving voiding problems, improving the peak urinary flow rate, and reducing the post-void residual urine than the placebo or MAT alone.

Plasmakinetic system

Plasmakinetic enucleation of the prostate (PKEP) with plasmakinetic resection of the prostate (PKRP)

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance review

An RCT (299) compared the safety and efficiency of plasmakinetic enucleation of the prostate (PKEP) with plasmakinetic resection of the prostate (PKRP) in 310 men with BPH. PKEP had longer operative time for prostate volume ≤ 60 mL but reduced operative time and blood loss for prostate volume > 60 mL. However, the incidence of transient incontinence after PKEP was higher irrespective of prostate size. The postoperative improvement in IPSS, quality of life, and maximal flow rate was similar at 24-month follow-up.

Plasmakinetic vapor enucleation of the prostate (PVEP) versus PKRP

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance review

An RCT (299) evaluated the efficiency of plasmakinetic vapor enucleation of the prostate (PVEP) with plasmakinetic resection of the prostate (PKRP) in 112 men with BPH. PVEP reported to be superior to PKRP in terms of operation time, haemoglobin loss, serum sodium

decrease, catheterisation duration and hospital stay. The maximum urinary flow rate, IPSS, post-void residual urine volume, quality of life score, transient incontinence, and urethral stricture at 3 months were similar in two groups.

An RCT (300) evaluated the efficacy and outcomes of plasma kinetic vaporisation (PKVP) and plasmakinetic resection (PKR) to treat BPH in 183 men. When compared with PKRP, PKR provided a shorter catheter duration and less bleeding and similar IPSS and maximum urine flow rate improvements after 1 year.

Diode laser enucleation of the prostate (DiLEP) versus plasmakinetic enucleation of the prostate (PKEP) and plasmakinetic resection of the prostate (PKRP)

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance review

An RCT (301) compared the efficacy and safety of diode laser enucleation of the prostate (DiLEP) with plasmakinetic enucleation of the prostate (PKEP) in 80 men with BPH and prostate volume > 80 mL. Compared with PKEP, patients treated with DiLEP showed a lower risk of blood loss, shorter bladder irrigation and catheterisation times, as well as shorter hospital stays. The operation time of the DiLEP group was longer than of PKEP group.

An RCT (302) assessed diode laser enucleation of the prostate (DiLEP) and plasmakinetic resection of the prostate (PKRP) for BPH in 152 men. DiLEP and PKRP were similar in efficacy and safety

for relieving obstruction and low urinary tract symptoms. IPSS, QoL, maximum urine flow rate, and PVR were similar for both procedures at 12 postoperative months. However, compared with PKRP, DiLEP had significantly decreased risk of haemorrhage, operative time, bladder irrigation time, catheterisation duration and hospital stays.

Implantable nitinol device

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance review

A systematic review (303) of two studies assessed the efficacy of temporary implantable nitinol device (TIND) for improving LUTS symptoms. IPSS was improved by 41% after 12 months and slightly worsened after 36 months compared to baseline values. Maximum urine flow rate increased by 4.4 ml/s after 12 months and did not decrease significantly after 36 months.

Radiofrequency (RF) water vapor thermal therapy

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance review

An RCT (304) evaluated the efficacy of water vapor thermal therapy with the Rezum System in 197 men with BPH and prostate size 30 to 80 cc. Convective water vapor thermal therapy provided better and rapid improvements in BPH symptoms compared with the control (rigid

cystoscopy) at 2 weeks and 3-month follow-up.

An RCT (305) reported 2-year outcomes plus 1-year results of a crossover trial after treatment with convective radiofrequency water vapor thermal energy. 197 men with BPH and prostate size 30 to 80 cc were randomised to thermal therapy with the Rezum System or a control group (Rigid cystoscopy with simulated active treatment). Convective radiofrequency water vapor thermal therapy improved urinary symptoms over control at 3 months and provided a sustained 51% reduction from baseline at 24 months. IPSS, flow rate and quality of life measures were markedly improved after thermal therapy compared with the control procedure.

An RCT (306) evaluated the efficacy of convective radiofrequency water vapor thermal therapy for treatment of moderate to severe LUTS due to BPH in 197 men with prostate volume 30 to 80 cc. Rigid cystoscopy with simulated active treatment sound effects served as the control. Compared with the control the IPSS improved (160%) after radiofrequency (RF) water vapor thermal therapy at 3 months. At least 50% improvement in IPSS, quality of life, maximum urine flow rate, and BPH Impact Index sustained up to 3 years. No late-related adverse events occurred, and no de novo erectile dysfunction was reported.

An RCT (307) assessed the water vapor thermal therapy for treatment of moderate to severe LUTS due BPH in 135 men. Lower urinary tract symptoms (ISSP 47%, quality of life 43%, maximum urine flow

rate 50%, BPH Impact Index 52%) were improved within 3 months after thermal therapy and sustained throughout 4 years.

An RCT (308) assessed the efficacy of the water vapor thermal therapy for improving lower urinary tract symptoms and erectile function in 197 men with BPH and volume prostate of 30 to 80 ml. Compared with rigid cystoscopy (control group), convective water vapor thermal therapy provided sustainable improvements for 12 months to lower urinary tract symptoms and urinary flow while preserving sexual functions.

Aquablation

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance review

A systematic review (309) of 1 RCT (n=184) compared the effects of aquablation and TURP for the treatment of LUTS in men with BPH and a prostate volume up to 80 mL. Based on short-term (up to 12 months) follow-up, the effect of aquablation on urological symptoms and quality of life was similar to TURP.

An RCT (310) assessed the safety and efficacy of aquablation and TURP for the treatment of LUTS in 181 men with BPH. BPH symptom score improvements were similar across the two groups. In both groups, mean maximum urinary flow rates increased markedly postoperatively.

An RCT (311) assessed the efficacy of aquablation versus TURP for the treatment of LUTS in 90 men with BPH. Change in IPSS at 1 year between aquablation and

TURP was similar (14.5 versus 13.8, respectively) but with a lower risk of adverse events and sexual dysfunction in aquablation group.

Prostatic artery embolisation (PAE)

Previous surveillance summary

No relevant evidence was identified.

2019 surveillance review

A meta-analysis (312) of 6 RCTs assessed the efficacy of Prostatic artery embolisation (PAE) in men with BPH. PAE improved maximum urine flow rate, PVR, IPSS, and QoL at 12 months, with a low incidence of serious adverse effect (0.3%).

A systematic review and meta-analysis (313) of 20 studies evaluated the efficacy and safety of PAE for treatment of moderate to severe LUTS and BPH. Improvements in IPSS, QoL score, PSA level, maximum urine flow rate, and PVR was reported following PAE. Major complications following PAE included pain in the perineum and retropubic area (9.4%) and haematuria (9.0%).

A systematic review (314) of 13 studies (total n=1,254) evaluated efficacy and safety of PAE for treatment of LUTS in men with BPH. Improvements of all investigated outcomes (IPSS, QoL), International Index of Erectile Function, prostate volume (PV), PSA, maximum urine flow rate, post-void residual) were seen at 12-month follow-up.

A systematic review (315) of 10 studies (total n=788) evaluated efficacy and safety of PAE for treatment of LUTS and BPH. At 6 months follow-up PV, PVR, maximum

urine flow rate, IPSS, and QoL were improved, while there was no major change in PSA. At 12 and 24 months, PV, PSA, PVR, maximum urine flow rate, IPSS, and QoL were improved.

A systematic review and metanalysis (316) of 5 studies (total n=708) evaluated efficacy and safety of PAE versus established surgical therapies. Mean reduction in the IPSS was lower after PAE compared with standard surgical therapies (mean difference 3.80 points). PAE was less efficient regarding improvements in all functional parameters assessed including maximum urinary flow, post void residual, and reduction of prostate volume. However, fewer adverse events occurred after PAE.

A systematic review (317) of 7 studies (total n=562) assessed the safety and efficacy of PAE for treatment of BPH. IPSS, quality of life, post-void residual measurement and PSA decreased from baseline at 6 months. Peak urinary flow rate increased from baseline at 6 months and total prostate volume decreased from baseline at 12 months. There were 200 minor complications and 1 major complication.

Prostatic urethral lift (PUL)

Previous surveillance summary

No evidence was identified at the 2012 Evidence update. The 2014 review identified 2 RCTs(318,319) comparing prostatic urethral lift with sham, reported improvement in symptoms from baseline up to 12 months.

2019 surveillance review

A systematic review (320) of 10 studies assessed the efficacy of PUL for treatment of LUTS. The pooled estimates from 452 and 680 patients suggested that, IPPS, maximum flow rate, and quality of life were improved following prostatic urethral lift (PUL). Sexual function was preserved with a small improvement estimated at 12 months. The authors indicated that pooled estimates were heterogeneous across the study groups.

A systematic review (321) of 6 studies assessed the efficacy and safety of the PUL for treating LUTS in men aged 65-74.3 years with prostate volume of 41cc-55cc. Improvements were found in IPSS, Benign Prostatic Hyperplasia Impact Index (BPHII), maximum urinary flow, post-void residual volume and quality of life up to 24 months. The adverse effects were mild.

A cross over RCT (322) evaluated the 24-month effectiveness of PUL procedure in men with LUTS and BPH. At 24 months after crossover to PUL, the IPSS, QoL, BPH Impact Index, and maximum urinary flow rate improved 36%, 40%, 54%, and 77% from baseline, respectively. Symptom response after the sham procedure indicated initial improvement at 1 month with significant decline by 3 months. Adverse events were mild to moderate.

An RCT (323) compared efficacy and safety of PUL to TURP in 80 men with BPH. Sexual function and quality of life were superior with PUL and significant symptom relief was achieved in both treatment arms.

An RCT (319) assessed the efficacy of PUL versus blinded sham control in 206 men

(prostatic urethral lift [n=140] versus sham control [n=6]) with BPH and prostate volume 30cc-80cc. The prostatic urethral lift reduced American Urological Association Symptom Index (AUASI) significantly at 2 weeks, 3 months and 12 months and improved peak urinary flow rate at 3 and 12 months. Adverse events were mild and transient. Further analysis of the same RCT in two years later (324) suggested that prostatic urethral lift preserved sexual function and provided rapid improvement in LUTS symptoms and quality of life up to 2 years. A further 3 years analysis (325) suggested that average improvements from baseline through 3 years were significant for total IPSS (41.1%), quality of life (48.8%), and individual IPSS symptoms. Ten percent (10%) of patients originally randomised to PUL required surgical re-intervention for treatment failure within the first 3 years.

A cross over study (326) assessed the clinical effect of the PUL on LUTS in men with prostate volume of 30-80 mL. LUTS symptoms, HRQL and sexual function were markedly improved after PUL compared with the sham procedure and sustained over the 12 months. Adverse events associated with the procedure were mild to moderate; only one patient (2%) required re-intervention with transurethral resection of the prostate in the first year.

An RCT (327) assessed the efficacy of PUL compared with blinded sham control in men with BPH and prostate volume 30cc-80cc. IPSS improvement after PUL was 88% greater than that of the sham at 3 months. LUTS and QoL were significantly improved by 2 weeks with return to

preoperative physical activity within 8.6 days. Improvement in IPSS, QoL, BPHII, and maximum urinary flow were durable through 5 years with improvements of 36%, 50%, 52%, and 44% respectively. Surgical re-treatment was 13.6% over 5 years. Adverse events were mild to moderate and transient.

Overall surgery

The 2014 review identified a systematic review (328) that found monopolar TURP reduced major morbidity in men with LUTS. The identified evidence indicated that TURP had similar efficacy compared with laser photoselection vaporisation, thulium laser vaporesction of the prostate, HoLEP, plasmaKinetic enucleation and transurethral incision of the bladder neck while there was no difference between monopolar or bipolar TURP.

A network meta-analysis (329) assessed efficacy and safety of TURP and laser surgeries for treatment of BPH. Holmium laser resection of the prostate (HoLRP) ranked the first best for IPSS at 6 months, and holmium laser enucleation of the prostate (HoLEP) ranked the first best at 12 months. For maximum urine flow rate at 6 and 12 months, HoLEP ranked the first best. For operative time TURP and for catheter removal time, diode laser enucleation of the prostate (DiLEP) ranked the first best.

A systematic review (330) of the 69 RCTs (total n=8,517) evaluated the efficacy and safety of transurethral ablative procedures for BPH. Bipolar TURP and monopolar TURP were comparable in terms of short-

term efficacy. However, bipolar TURP was associated with a lower rate of perioperative complications. HoLEP was associated with better short-term efficacy outcomes, fewer immediate complications, and a shorter hospital stay compared with monopolar TURP. GreenLight photoselective vaporization of the prostate was associated with a shorter hospital stay and fewer complications but no difference in short-term efficacy outcomes when compared with monopolar TURP.

Intelligence gathering

Topic experts commented:

- “There are new treatment modalities like Urolift, Rezum and prostate artery embolisation all separately approved by NICE but not incorporated as recommendation in LUTS care pathway.
- Superiority of HoLEP (Holmium Laser Enucleation of the Prostate) over TURP (Transurethral Resection of the Prostate) should be clearly mentioned in the guideline for surgical therapy in appropriate group of patients with large prostates in terms of less bleeding and transfusion rates.
- The current guideline needs to be updated as open prostatectomy is not the only choice in prostate size over 80 g. HoLEP can be used for prostates of any size and outcomes are superior compared

to open prostatectomy in terms of bleeding, transfusion rates, catheterisation time, hospital stay and convalescence’.

- There are new ‘Surgical management, particularly the use of laser vaporisation of the prostate (green light) and new techniques such as Urolift’ implant.
- Urolift could replace chronic drug therapy and a cost-QoL analysis will help to establish that intervention as a choice to replace initial drug therapy for BPH induced LUTS.”

Impact statement

Transurethral resection of the prostate (TURP)

TURP versus Photoselective vaporisation of the prostate (PVP)

Evidence from 2 systematic reviews, 2 metanalysis, 5 RCTs and 1 cost effective analysis identified in 2014 review suggests that photoselective vaporisation of prostate and TURP may have similar efficacy and safety in treatment of LUTS caused by BPH.

New evidence in current review from 1 systematic review and 6 RCTs suggests that the two interventions appeared equally improve IPSS, postvoidal residual and maximum urinary flow rate and Sexual Health Inventory for Men. Currently PVP is not mentioned in the guideline. As such, this new evidence has the potential to

impact upon the current recommendations.

This intervention has been covered in a related Medical technologies guidance MTG29: [GreenLight XPS for treating benign prostatic hyperplasia](#) [MTG29]. MTG29 is incorporated in LUTS care pathway.

Bipolar versus monopolar TURP

Evidence from an RCT in the 2012 Evidence update indicates that patients treated with bipolar TURP appear to have fewer readmissions compared with those treated with monopolar TURP. However, a systematic review showed that the two treatment modalities did not differ significantly with respect to operation times, transfusion rates, retention rates after catheter removal and urethral complications.

Evidence from 5 RCTs and 1 systematic review identified in the 2014 reported that monopolar and bipolar TURP both improved LUTS with no significant differences between the interventions.

New evidence from 7 RCTs and 2 systematic reviews in current review suggests no significant difference in short-term efficacy between the two treatment modalities. However, there was some suggestion that bipolar TURP may reduce bleeding and complications better than the monopolar TURP. This new evidence has the potential to impact upon the current recommendations which recommends both approaches.

TURP versus thulium laser vaporesction/resection of the prostate

Findings from 2 studies in 2014 review reported that thulium laser vaporisation of the prostate and TURP both improved LUTS with no significant difference between the interventions.

New evidence in current review from 3 RCTs and 2 systematic review indicates that thulium laser vaporisation/resection of the prostate and bipolar TURP may be comparable in improving IPSS, QoL, PVR, and maximum urine flow rate.

The current recommendation states that laser vaporisation techniques for managing voiding LUTS should only be offered as part of an RCT that compares these techniques with TURP. As such, this new evidence has the potential to impact upon the current recommendations.

TURP versus transurethral resection and holmium laser enucleation (HoLEP)

Evidence from 2 RCTs at 2012 Evidence update indicates that HoLEP and bipolar TURP were equally effective in treating patients with LUTS.

Evidence from 2014 review from 4 RCTs, 2 systematic review and 1 meta-analysis comparing HoLEP with TURP suggest that both surgical treatments may be similar in improving LUTS.

New evidence in current review from 2 systematic reviews and two RCTs suggests that HoLEP appeared to be associated with less blood loss, lower transfusion rates, and a shorter hospital stay but longer operative time and more postoperative dysuria. In one RCT HoLEP demonstrated long-term efficacy in

improving IPSS and urinary flow rate and quality of life compared with TURP.

Evidence from the studies is broadly consistent with current recommendations in CG97 which recommends either of these treatments. A topic expert commented that superiority of HoLEP over TURP should be clearly mentioned in the guideline for surgical therapy in appropriate group of patients with large prostates in terms of resulting in less bleeding and lower transfusion rates. As such, this new evidence has the potential to impact upon the current recommendations.

C-TURP (channel TURP) combined with interstitial laser coagulation

Evidence from an RCT at 2014 review suggests that (C-TURP) combined with an interstitial laser coagulation appears safe and effective for treatment of BPH. No evidence was identified at the current review.

Current evidence on the efficacy and safety of procedure-TURP is inadequate to support its use as an alternative to TURP in treating LUTS.

TRUP versus transurethral plasma kinetic enucleation of the prostate (TPKEP)

One RCT (current review) indicated that PlasmaKinetic enucleation of the prostate was associated with less blood loss, shorter hospital stays, and reduced catheterisation time compared with bipolar transurethral resection of the prostate. One RCT (current review) reported that IPSS, Maximum urine flow rate and PVR

equally improved in both groups at six months follow-up.

Current evidence on the efficacy and safety of TPKEP is inadequate to support its use as an alternative to TURP in treating LUTS.

TURP versus transurethral enucleation of the prostate (TUERP)

One RCT (2014 review) indicated that TUERP appeared better than TURP with higher resection rate of the prostate, shorter operation time and bladder irrigation time, less intraoperative blood loss, fewer postoperative complications, and faster recovery. TUERP appeared better than TURP in 1 RCT (current review) with higher resection rate of the prostate, shorter operation time and bladder irrigation time, less blood loss, fewer postoperative complications, and faster recovery.

Current evidence on the efficacy and safety of TUERP is inadequate to support its use as an alternative to TURP in treating LUTS.

TURP versus 'button type' bipolar plasma vaporisation (BTPV):

One RCT (2014 review) reported the superiority of bipolar plasma vaporisation of the prostate with 'button type' electrode over standard TRUP in improving LUTS. One systematic review (current review) noted that the improvement in urinary symptoms and overall complications in BTPV were comparable to conventional TURP. Current evidence on the efficacy and safety of BTPV is inadequate to support its

use as an alternative to TURP in treating LUTS.

TURP versus transurethral incision of the bladder neck

One RCT (2014 review) found that at 6 months postoperatively, no significant difference in IPSS was observed between the two groups although the maximum urine flow rate in patients receiving STRUP plus TUIBN was markedly higher than in those receiving TURP.

Current evidence on the efficacy and safety of IPSS is inadequate to support its use as an alternative to TURP in treating LUTS.

TURP versus prostatic artery embolisation (PAE)

Two systematic reviews (current review) reported that TURP improved maximum urine flow rate and QoL and decreased prostate volume better than PAE. Postoperative IPSS and complications were similar in both groups. One RCT (current review) indicated that TURP group showed greater degrees of improvement in the IPSS, QoL, peak urinary flow, and postvoiding residual urine volume at 1 and 3 months, when compared with the PAE group.

This intervention has been covered in a related Interventional procedures guidance and incorporated in LUTS care pathway:

[Prostate artery embolisation for lower urinary tract symptoms caused by benign prostatic hyperplasia](#) (April 2018) [IPG611]

TURB versus transurethral resection in saline (TURis):

One RCT (current review) reported that TURis bipolar vaporisation had a longer operative time than monopolar TURP. Postoperatively, the TURis group had a shorter catheter time and a shorter length of hospital stay. Quality of life score was similar in two groups at 3 and 6 months.

TURis is not included in the guideline but has been covered in a related Medical technologies guidance and incorporated in LUTS care pathway:

[The TURis system for transurethral resection of the prostate](#) (February 2015) MTG23

TURP versus transurethral vaporisation of the prostate (TUVV):

One RCT (2014 review) found no significant differences on safety and effectiveness of transurethral vaporisation of the prostate (TUVV) compared with the standard transurethral resection of the prostate (TURP) in the treatment of BPH. One systematic review and 1 RCT (current review) indicated that the TUVV group had significantly lower mean values of operative time, hospital stay, catheterisation period, irrigation fluid volume and serum haemoglobin, compared with TURP group.

Current evidence on the efficacy and safety of TUVV is inadequate to support its use as an alternative to TURP in treating LUTS.

TURP versus GreenLight XPS Laser (GLP-XLS)

One RCT (current review): The long-term effectiveness and safety of GLP-XLS on IPSS, maximum urine flow rate, PSA, prostate volume, overactive bladder) was equivalent to conventional TURP for the treatment of LUTS.

GLP-XLS is not included in the guideline but has been covered in a related Medical technologies guidance and incorporated in LUTS care pathway:

[GreenLight XPS for treating benign prostatic hyperplasia](#) [MTG29] Published: June 2016

C-BPVP, S-BPVP, M-TURP

One RCT (current review) reported that both C-BPVP and S-BPVP and had better perioperative safety and improved follow-up voiding and symptom scores than M-TURP.

Current evidence on the efficacy and safety of C-BPVP and S-BPVP is based on a single study therefore inadequate to support their use as an alternative to TURP in treating LUTS.

TURP compared with medications

One RCT (2014 review) indicated that both interventions improved study outcomes although TURP was associated with a significant improvement in the number of nocturnal awakenings and quality of life in comparison with tamsulosin.

The guideline recommends that surgical options should only be offered if other treatments have failed and currently there

is insufficient new evidence to change this recommendation.

Holmium laser enucleation of the prostate (HoLEP)

Holmium laser vs conventional monopolar electrocautery (C-BNI)

One RCT (current review) reported that maximum urine flow rate and American Urological Association Symptom Score at each follow-up, and maximum urine flow rate, and post-void residual at 6 months were comparable between two groups.

HoLEP versus plasmakinetic enucleation and resection of the prostate

One RCT (2014 review) indicated that compared with plasmakinetic enucleation, laser enucleation of the prostate had significantly shorter operative time, postoperative irrigation, time and catheterisation time. One RCT (2014 review) reported that the postoperative improvement in IPSS, QoL, maximal flow rate and post-void residual urine volume was similar in both groups at 1, 6, 12 and 24 months but significantly better in the enucleation group at 36, 48 and 60 months.

HoLEP versus thulium laser transurethral enucleation of the prostate

One RCT (2014 review) reported that at 18 months, the lower urinary tract symptoms were improved significantly in both groups compared with the baseline values. Two RCTs (current review) indicated that at 1-month follow-up, peak urinary flow rates, post-void residual volumes, IPSS, QoL had improved

significantly from baseline without significant differences between the groups.

HoLEP versus Laser photoselective vaporisation of the prostate

One RCT (2012 Evidence update) reported no differences in laser vaporisation and TURP in IPSS reductions or maximum urine flow rate in men with LUTS caused by BPH. A cost effectiveness study (2012 Evidence update) based on the UK healthcare setting indicated that initial ablation with diathermy vaporisation, followed by HoLEP for treatment failures, had an 85% probability of being cost effective at £20,000 per quality adjusted life year.

Two RCTs (2014 review) indicated that photoselective vaporisation of the prostate was equally effective and safe as holmium laser ablation of the prostate in men with BPH. High-power photovaporisation of the prostate can achieve and maintain the same results as TURP over a period of 24 months for LUTS caused by BPH.

HoLEP versus transurethral electrovaporisation resection of the prostate (TUEVP)

One RCT (current review) indicated that at 2 weeks and 3 months following the surgery the incidence of stress incontinence in HoLEP group were both lower than those in TUEVP group, while there was no significant difference on the IPSS and maximum urine flow rate at 3-month follow-up after the surgery.

Thulium laser resection

Evidence for following interventions was identified:

Thulium laser resection of the prostate-tangerine technique (TmLRP-TT) versus plasmakinetic resection of the prostate (PKRP)

One RCT from current review (283) indicated that the TmLRP-TT treatment was followed by a lower haemoglobin drop, shorter catheterisation time and hospital stay compared with treatment with PKRP.

ThuLEP versus plasmakinetic enucleation of the prostate (PKEP)

One RCT (current review) reported that the 12-month follow-up showed no difference in urinary parameters between the two groups.

ThuRP versus plasmakinetic resection of the prostate (PKRP)

One systematic review (current review) reported that the postoperative data (IPSS, maximum urine flow rate, post-void residual urine volume, severe bleeding, temporary urinary retention, temporary incontinence, urinary tract infection, and urethral stricture) did not differ significantly.

Thulium laser resection is not included and recommended in the current guideline. The guideline recommends that if surgery is offered for managing voiding LUTS then HoLEP should be one of the methods offered. As such, this new evidence has the potential to impact upon the current recommendations.

Transurethral microwave thermotherapy

Evidence identified at 2014 review from a Cochrane systematic reported that the pooled mean urinary symptom scores decreased by 65% with TUMT and by 77% with TURP.

The guideline recommendation states that transurethral microwave thermotherapy should not be offered as an alternative to TURP, TUVP or HoLEP and no new evidence was identified which would change the recommendation.

Prostatectomy

Evidence for following interventions was identified:

Transvesical open prostatectomy versus plasma enucleation of the prostate

Two RCTs (2014 review) indicated that both treatment groups had a similar and significant postoperative improvement in quality of life, maximum uroflow rate, post-void residual urine volume and prostate specific antigen from baseline.

Transvesical prostatectomy versus transurethral enucleation and resection of the prostate

One RCT (2014 review) reported that both interventions had similar efficacy for treatment of LUTS in men with BPH.

Bipolar transurethral plasmakinetic prostatectomy versus thulium laser resection of the prostate

One RCT (2014 review) reported similar and significant postoperative improvement in both groups for IPSS, QoL, maximum

urine flow rate and PVR at 3 months after the operation.

Open prostatectomy versus bipolar transurethral resection of the prostate

One RCT (2014 review) indicated that IPSS symptom score, IIEF-5 and QoL, PSA, peak urinary flow rates and post-void residual urine volume in the 2 groups were similar.

Open prostatectomy versus holmium laser enucleation of the prostate (HoLEP):

One systematic review (current review) indicated that peak urinary flow rate, post-void residual urine volume, IPSS and quality of life at 12 and 24 months were similar in the two intervention groups.

Transurethral enucleation and resection of the prostate (TUERP) and transvesical prostatectomy (TVP)

One RCT (current review) indicated that patients with prostate volumes >80 mL who underwent TUERP had shorter catheterisation times and hospital stays. IPSS, PVR, maximum urine flow rate or QoL scores were comparable at 3 and 12 months and adverse events were similar in the two groups.

B-TURP versus laparoscopic simple prostatectomy (LSP)

One RCT (current review) reported that at 1, 3, 6, and 12 months postoperatively, improvement was similar in post-void residual urine volume, maximum urine flow rate, and IPSS between the two groups.

Thulium laser prostatectomy (TmLRP) versus TURP

One RCT (current review) reported that during the 1, 3, and, 12 months of postoperative follow-up, the procedures did not show a significant difference in IPSS, QoL, maximum urine flow rate, and PVR.

Plasmakinetic enucleation of the prostate (PKEP) versus open prostatectomy

Evidence from an RCT in current review indicated that PKEP had long-term micturition improvement equivalent to open prostatectomy and lower perioperative morbidity.

The current recommendation states that open prostatectomy should only be offered as an alternative to TURP, TUVP or HoLEP to men with prostates estimated to be larger than 80g. The identified new evidence suggests that open prostatectomy may have similar or better efficacy compared with alternatives surgeries in men with BPH. Therefore, new evidence may impact the current guideline recommendations.

Other laser treatments

Diode laser enucleation of the prostate (DiLEP) to Bipolar endoscopic enucleation of the prostate (BEEP)

One RCT (current review) indicated that DiLEP was comparable to BEEP regarding maximum urine flow rate, and IPSS at 12 months.

Laparoscopic adenomectomy (LA) and Eraser laser enucleation of the prostate (ELEP)

One RCT (current review) indicated that the two groups were comparable in IPSS scores and maximum urine flow rate throughout the follow-up period.

Auriculotherapy (AT) using laser AT (LAT) and magneto-AT (MAT)

One RCT (current review) indicated that a combined AT approach was associated with greater improvements in relieving voiding problems, improving the peak urinary flow rate, and reducing the post-void residual urine than the placebo group or MAT alone.

Currently laser treatments are not recommended in the guideline. As such, this new evidence has the potential to impact upon the current recommendations.

Plasmakinetic system

No evidence was identified at the previous reviews. Evidence from following interventions was identified at the current review:

Plasmakinetic enucleation of the prostate (PKRP) versus open prostatectomy (OP)

One RCT reported that PKEP showed long-term micturition improvement equivalent to OP and lower perioperative morbidity

Plasmakinetic enucleation of the prostate (PKEP) with plasmakinetic resection of the prostate (PKRP)

One RCT indicated that improvement in ISPP, quality of life, and maximal flow rate was similar at 24-month follow-up.

Plasmakinetic vapor enucleation of the prostate (PVEP) versus PKRP

Two RCTs reported that the improvement in maximum urinary flow rate, IPSS, post-void residual urine volume, quality of life score, transient incontinence, and urethral stricture at 3 months was similar. Currently PVEP and PKRP are not mentioned in the guideline. As such, this new evidence has the potential to impact upon the current recommendations.

Diode laser enucleation of the prostate (DiLEP) versus plasmakinetic enucleation of the prostate (PKEP) and plasmakinetic resection of the prostate (PKRP)

Findings from 2 RCTs in current review reported that patients treated with DiLEP had a lower risk of blood loss, shorter bladder irrigation and catheterisation times, as well as shorter hospital stays compared with PKEP and PKRP. However, DiLEP and PKRP were similar in efficacy and safety in improving LUTS.

Currently Plasmakinetic systems are not mentioned in the recommendations. As such, this new evidence has the potential to impact upon the current recommendations.

Implantable nitinol device

No evidence was identified at the previous reviews. New evidence from a systematic review of 2 studies suggests that implantable nitinol device may improve LUTS symptoms in men with BPH.

This intervention is not included in the guideline but has been covered in a related Interventional procedures guidance and incorporated in LUTS care pathway:

[Prostatic urethral temporary implant insertion for lower urinary tract symptoms caused by benign prostatic hyperplasia](#) (January 2019) [IPG641]

Radiofrequency (RF) water vapor thermal therapy

No evidence was identified at the previous reviews. New evidence from 5 RCTs in current review suggests that convective radiofrequency thermal therapy with the Rezum System may provide sustainable improvement for LUTS.

This intervention has been covered in a related Medtech innovation briefing MIB158 and incorporated in LUTS care pathway: [Rezum for treating benign prostatic hyperplasia](#) [MIB158].

Aquablation

New evidence from 3 RCTs indicates that change in IPSS between aquablation and TURP appeared similar after one year but with a lower risk of adverse events and ejaculatory dysfunction in aquablation group.

This intervention has been covered in 2 related Interventional procedures guidance and incorporated in LUTS care pathway:

[Transurethral water jet ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia](#) (September 2018) [IPG629]

[Transurethral water vapour ablation for lower urinary tract symptoms caused by](#)

[benign prostatic hyperplasia](#) (August 2018) [IPG625]

Prostatic artery embolisation (PAE)

No evidence was identified at the previous reviews. New evidence from 3 systematic reviews and one meta-analysis of RCTs suggests that IPSS, QoL score, PSA level, PV, maximum urine flow rate and PVR may improve following PAE. One further systematic review indicated that PAE was less efficient in improving maximum urinary flow, post void residual, and reduction of prostate volume.

This intervention is not included in the guideline but has been covered in a related Interventional procedure guidance and incorporated in LUTS care pathway:

[Prostate artery embolisation for lower urinary tract symptoms caused by benign prostatic hyperplasia](#) (April 2018) [IPG611]

Prostatic urethral lift (PUL)

Evidence from 2 RCTs at 2014 review suggests that prostatic urethral lift may improve LUTS in men with BPH. Evidence from 2 systematic current review and 5 RCTs are also supporting the use of PUL in men with prostate size of 30cc to 80cc.

This intervention has been covered in a related Interventional procedure guidance IPG475 and incorporated in LUTS care pathway:

[Insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia](#) (published January 2014).

A topic expert commented that urolift could replace chronic drug therapy. We

did not identify any new evidence comparing urolift surgery to a medical treatment. The Interventional Procedure guidance (IPG475) recommends that the current evidence on the efficacy and safety of insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia is adequate to support the use of this procedure.

Overall surgery

The evidence identified at 2014 review from one RCT suggests that TURP may have similar efficacy compared with laser photoselection vaporisation, thulium laser vaporesction of the prostate, HoLEP, plasmaKinetic enucleation and transurethral incision of the bladder neck while there was no difference between monopolar or bipolar TURP.

New evidence from a network meta-analysis from current review ranked holmium laser resection of the prostate (HoLRP) the first best for improving IPSS at 6 months and holmium laser enucleation of the prostate (HoLEP) for improving IPSS at 12 months. HoLEP was also ranked for first best in improving maximum urine flow rate at 6 and 12 months.

The guideline recommends that if offering surgery for managing voiding LUTS, monopolar or bipolar TURP, monopolar transurethral vaporisation of the prostate or HoLEP should be offered. We identified a large body of evidence in current review on newer interventions and surgical treatments including Urolift, Rezum and laser vaporisation for treatment of voiding symptoms of LUTS which are not

addressed in the current guideline. Some of these new procedures are covered in other NICE guidance and advice, and are incorporated in the NICE pathway for '[Managing lower urinary tract symptoms in men](#)'. Topic experts indicated that the recommendations no longer support current practice as more treatment options, including advances in technology and new surgical procedures, have become available since the guideline was published in 2010.

These changes suggest a need to update the guideline so that it remains relevant to clinical practice in the UK. In addition, a comprehensive single piece of guidance would be most useful for healthcare professionals.

New evidence identified that may change current recommendations.

[1.6 Surgery for storage symptoms](#)

Recommendations in this section of the guideline

- 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.
- 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.
- 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).
- 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.

- 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.
- 1.6.6 Do not offer myectomy to men to manage detrusor overactivity.
- 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.
- 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.
- 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.

* At the time of publication (June 2015), botulinum toxin A and botulinum toxin B did not have UK marketing authorisations for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

Surveillance proposal

No new information was identified at any surveillance review.

These recommendations should not be updated.

Surgery for storage symptoms

Botulinum toxin

Idiopathic detrusor overactivity

previous surveillance summary

No new evidence was identified at the 2012 Evidence update. Findings from the two systematic reviews (331,332) and two RCTs (333,334) identified at 2014 review indicated that botulinum toxin has a

positive effect on idiopathic detrusor overactivity.

2019 surveillance summary

A systematic review (335) of 3 studies (study duration ranged from 8 to 24 weeks, total n=522) assessed the efficacy and safety of botulinum toxin type A compared with placebo for LUTS. The pooled overall standard mean difference in IPSS, and change in maximum urinary flow, prostate volume, and post-voided residual

volume were similar between the two groups.

A phase III RCT (336) assessed the efficacy, safety of onabotulinumtoxinA (BOTOX; 100U dose injection) treatment in 548 patients with overactive bladder and urinary incontinence who were inadequately managed by antimuscarinics. At week 12, onabotulinumtoxinA significantly decreased urinary incontinence episodes per day (-2.95 versus -1.03). OnabotulinumtoxinA 100 U was well tolerated and improved all other overactive bladder symptoms, patient reported benefit, and health-related quality of life.

An RCT (337) assessed the efficacy and safety of Botulinum Neurotoxin Type A (BoNT-A) prostatic injection (n=64) versus medical (n=63) therapy in patients with LUTS due to BPH. At 4 months, mean IPSS score in the BoNT-A group was comparable to with control.

An RCT (338) assessed the efficacy and tolerability of onabotulinumtoxinA 200 U vs placebo to treat LUTS and BPH in 315 men previously treated with oral medication in a 24-week phase II trial. Decreases from baseline in IPSS were observed in the onabotulinumtoxinA and placebo groups (-6.3 vs -5.6 points). Adverse events were similar between the two treatment groups.

An RCT (339) compared the efficacy and safety of onabotulinumtoxinA or solifenacin versus placebo in patients with overactive bladder who had urinary incontinence an inadequate response to or were intolerant of an antimuscarinic. The

change from baseline in incontinence episodes per day was significantly greater with onabotulinumtoxinA or solifenacin versus placebo. OnabotulinumtoxinA showed significantly greater decreases in urinary incontinence than solifenacin with a third of patients achieving a 100% incontinence reduction. No unexpected safety indications were observed. Urinary tract infection in 25.5% of cases and urinary retention in 6.9% were more common with onabotulinumtoxin A.

An RCT (340) evaluated the efficacy of OnabotulinumtoxinA for treatment of 557 patients with overactive bladder and urinary incontinence inadequately managed with antimuscarinics. OnabotulinumtoxinA significantly decreased the daily frequency of urinary incontinence episodes versus placebo and 22.9% versus 6.5% of patients became completely continent. All other overactive bladder symptoms improved versus placebo. OnabotulinumtoxinA improved patient health-related quality of life across multiple measures.

A meta-analysis (341) of 2 phase III RCTs (total n=1,105) evaluated the impact of onabotulinumtoxinA on individual domains of the quality of life. At 12 weeks of treatment, onabotulinumtoxinA 100U demonstrated significant improvements versus placebo in incontinence QoL, Incontinence Quality of Life subscale scores and all domains of the King's Health Questionnaire.

An RCT (342) assessed whether catheter instillation of 200 U onabotulinumtoxinA formulated with liposomes is safe and effective for the treatment of overactive

bladder. At 4 weeks after the treatment, a single intravesical instillation of lipo-botulinum toxin was associated with decreases in overactive bladder symptoms (micturition events, urgency severity scores) compared with placebo. The effects of lipo-botulinum toxin on urinary urge incontinence were inconclusive.

Overactive bladder

previous surveillance summary

No new evidence was identified at the 2012 Evidence update. Three systematic reviews (343–345) and 4 RCTs (346–349) from 2014 review indicated a potential beneficial effect of botulinum toxin compared with placebo on overactive bladder symptoms.

2019 surveillance summary

No relevant evidence was identified.

BPH

previous surveillance summary

No new evidence was identified at the 2012 Evidence update. The 2014 review identified two RCTs (350,351) which found no significant difference between different doses of botulinum toxin (100 U versus 200 U and 100 U versus 300 U) for LUTS treatment associated with BPH. However, a post-hoc analysis an RCT (352) identified at 2014 review found a significant reduction in IPSS compared with placebo with botulinum toxin 200 U in prior alpha blocker users.

2019 surveillance summary

No relevant evidence was identified.

Surgery in reducing storage symptoms

Previous surveillance summary

No new evidence was identified at the 2012 Evidence update. The 2014 review identified a systematic review (353) that assessed the potential additional benefit of non-standard versus standard surgical treatments for BPH and concluded that there was a lack of high quality RCTs and trials designed to investigate noninferiority. A second systematic review (354) reported that the implantation of an artificial urinary sphincter improved continence in men with non-neurogenic stress urinary incontinence.

2019 surveillance summary

No relevant evidence was identified.

Posterior tibial nerve stimulation

Previous surveillance summary

No new evidence was identified at the 2012 Evidence update.

The 2014 review identified 2 systematic reviews (355,356) and 1 RCT (357) on electrical stimulation for urinary incontinence. The results were mixed with one review reporting that electrical stimulation did not improve recovery of urinary incontinence better than pelvic floor muscle training while the second review identified some evidence that electrical stimulation had a short-term effect in reducing incontinence compared with sham treatment at six months but not at 12 months. Finding from the RCT (357) showed that urodynamic results improved following posterior tibial nerve stimulation in patients with nocturnal enuresis.

2019 surveillance summary

No relevant evidence was identified.

Intelligence gathering

No new information was identified.

Impact statement

Botulinum toxin

Idiopathic detrusor overactivity

Findings from the 2 systematic reviews and 2 RCTs identified at 2014 review indicated that botulinum toxin has a positive effect on idiopathic detrusor overactivity. Evidence from 6 RCTs and 2 systematic review in current review is also supports the use of onabotulinumtoxinA for treatment of urinary incontinence and detrusor overactivity.

This new evidence is unlikely to impact on the guideline as a bladder wall injection with botulinum toxin is already recommended for men with detrusor overactivity who have not responded to conservative management and drug treatment.

Overactive bladder

No new evidence was identified at the 2012 Evidence update. Three systematic reviews and 4 RCTs from 2014 review indicated a potential beneficial effect of botulinum toxin compared with placebo on overactive bladder symptoms.

The guideline algorithm indicates that injection of botulinum into the bladder wall may be considered in men with symptoms of overactive bladder after conservative

management and antimuscarinics have failed and the identified new evidence supports this approach.

BPH

No new evidence was identified at the 2012 Evidence update. The 2014 review identified two RCTs which found no significant difference between different doses of botulinum toxin for LUTS treatment associated with BPH. However, an RCT identified at 2014 review found a significant reduction in IPSS compared with placebo with botulinum toxin 200 U in prior alpha blocker users.

Botulinum toxin injection into the prostate for managing voiding LUTS is only recommended as part of an RCT and currently there is insufficient consistent new evidence to impact this recommendation.

Surgery in reducing storage symptoms

No new evidence was identified at the 2012 Evidence update. The 2014 review identified a systematic review that concluded that there was a lack of high quality RCTs and trials designed to investigate non-standard versus standard surgical treatment for BHP. A second systematic review that was identified at 2014 review reported that the implantation of an artificial urinary sphincter improved continence in men with stress urinary incontinence.

Implantation of an artificial sphincter to manage stress urinary incontinence in men whose symptoms have not responded to conservative management and drug treatments is already recommended and

the identified new evidence is unlikely to change the direction of this recommendation.

Posterior tibial nerve stimulation

Evidence from 2 systematic reviews and 2 RCT from 2014 and current review suggests that electrical stimulation may have a short-term effect in reducing incontinence.

This intervention is not included in the guideline but has been covered in a related Interventional procedure guidance and incorporated in LUTS care pathway:

[Percutaneous posterior tibial nerve stimulation for overactive bladder syndrome](#) (October 2010) IPG362

New evidence is unlikely to change guideline recommendations.

1.7 Treating urinary retention

Recommendations in this section of the guideline

- 1.7.1 Immediately catheterise men with acute retention.
- 1.7.2 Offer an alpha blocker to men for managing acute urinary retention before removal of the catheter.
- 1.7.3 Consider offering self- or carer-administered intermittent urethral catheterisation before offering indwelling catheterisation for men with chronic urinary retention.
- 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/percussable bladder).
- 1.7.5 Catheterise men who have impaired renal function or hydronephrosis secondary to chronic urinary retention.
- 1.7.6 Consider offering intermittent or indwelling catheterisation before offering surgery in men with chronic urinary retention.
- 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.
- 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.
- 1.7.9 Continue or start long-term catheterisation in men with chronic retention for whom surgery is unsuitable.

- 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.

Surveillance proposal

No new information was identified at any surveillance review.

Intelligence gathering

No new information was identified.

1.8 Alternative and complementary therapies

Recommendations in this section of the guideline

- 1.8.1 Do not offer homeopathy, phytotherapy or acupuncture for treating LUTS in men.

Surveillance proposal

These recommendations should not be updated.

Alternative therapies

Phytotherapy

Serenoa repens

Previous surveillance summary

The 2012 Evidence update identified a systematic review ([Tacklind et al. 2009](#)) which found that Serenoa repens had positive effect on nocturia however, a sensitivity analysis showed that the findings were derived from small and old trials and were not supported by the larger newer trials. The 2014 review identified 7 studies (358–364) which 6/7 studies

reported no benefit of Serenoa repens over control while one study found reduction in IPSS in men with LUTS.

2019 surveillance summary

No relevant evidence was identified.

Cernilton

Previous surveillance summary

No new evidence was identified at the 2012 Evidence update. The 2014 review identified a systematic review (365) which found Cernilton was not more effective than placebo in improving urinary flow rates, residual volume or prostate size in men with BPH. However, an overview of

systematic reviews (362) in 2014 review observed a significant improvement in BPH symptoms following treatment with Cernilton.

2019 surveillance summary

No relevant evidence was identified.

Foods and supplements

Selenium and Silymarin

Previous surveillance summary

No new evidence was identified in the 2012 Evidence update. The results of an RCT (366) identified in the 2014 review, indicated a significant improvement in IPSS score, urodynamic parameters: maximal rate of urine flow, average flow, total PSA value and serum selenium levels in men with LUTS treated with a combination of selenium and silymarin.

2019 surveillance summary

No relevant evidence was identified.

Grape juice

Previous surveillance summary

No new evidence was identified in the 2012 Evidence update. The 2014 review identified an RCT (367) that found no difference in LUTS in men taking a daily 240 ml 100% grape juice versus placebo after 3 months.

2019 surveillance summary

No relevant evidence was identified.

Soy isoflavones

Previous surveillance summary

No new evidence was identified in the 2012 Evidence update. The 2014 review

identified an RCT (368) which assessed the efficacy and safety of soy isoflavones in controlling the symptoms and signs of LUTS and found a slight superiority of isoflavones over placebo over 12 months.

2019 surveillance summary

No relevant evidence was identified. Acupuncture

Laser acupuncture

Previous surveillance summary

No new evidence was identified in the 2012 Evidence update. The 2014 review identified two studies (369,370) on acupuncture for treatment of BPH or nocturnal enuresis. One study evaluated the efficacy of acupoint electroacupuncture while the second study assessed the effect of laser acupuncture on bladder reservoir function and enuresis frequency. No significant treatment effect compared to the control group was observed in either study.

2019 surveillance summary

No relevant evidence was identified.

Other alternative therapies

Biofeedback combined with physiokinesitherapy

Previous surveillance summary

No new evidence was identified in the 2012 Evidence update. The evidence from an RCT (23) in the 2014 review reported that preoperative biofeedback combined with an assisted low-intensity programme of postoperative perineal physiokinesitherapy had significantly improved incidence, duration and severity

of urinary incontinence in patients undergoing radical prostatectomy.

2019 surveillance summary

No relevant evidence was identified.

Tai chi (Chinese martial art)

Previous surveillance summary

No new evidence was identified in the 2012 Evidence update. Findings from an RCT (371) in the 2014 review showed Tai chi significantly improved QoL in men with LUTS. However, the study was small with a short-term follow-up.

2019 surveillance summary

No relevant evidence was identified.

Osteopathic treatment

Previous surveillance summary

No new evidence was identified in the 2012 Evidence update. One RCT (372) identified in the 2014 review found a significantly greater improvement in IPSS following osteopathic treatment compared to control.

2019 surveillance summary

No relevant evidence was identified.

Intelligence gathering

No relevant information was identified.

Impact statement

Phytotherapy

Over all findings from 8 studies at previous reviews suggest no benefit of Serenoa repens over control in improving LUTS. Findings from 2 systematic reviews and 3 RCTs indicate that extract of Serenoa

repens as monotherapy had a similar efficacy to tamsulosin and short-term 5alpha-reductase inhibitors. Findings from 2 further systematic reviews about benefits of Cernilton in LUTS was conflicting. No relevant evidence was identified in the current review.

Overall, the identified evidence is unlikely to change the direction of the current guideline recommendation which indicates that phytotherapy for LUTS in men should not be offered.

Foods and supplements

Evidence for following interventions was identified:

Selenium and Silymarin

One RCT (2014 review) reported that improvement in IPSS score, urodynamic parameters, maximal rate of urine flow, average flow, and total PSA value in men with LUTS treated with the intervention. 1 RCT in current review indicated that the combined treatment was more effective than single therapies in improving IPSS and maximum urine flow rate in patients with LUTS.

Pycnogenol versus l-arginine aspartate

One RCT (current review) indicated that improvement in IPSS and IPSS-QoL were similar between the two groups.

Calprost (extract of pumpkin seed oil) versus terazosin

One RCT (current review) reported that IPSS improved equally in both groups.

Roystonea regia (a species of palm) versus saw palmetto (fruit lipid extracts)

One RCT (current review) indicated that at two months and 24 weeks both treatments improved equally the total IPSS and post-voiding residual volume from baseline.

Grape juice

One RCT (2014 review) reported no difference in LUTS in men taking a daily 240 ml grape juice versus placebo after 3 months.

Soy isoflavones

One RCT (2014 review) reported a slight superiority of isoflavones versus placebo in LUTS treatment over 12 months.

Pumpkin seed

Two RCTs (current review) indicated that IPSS, uroflowmetry parameters and quality of life were improved following Cucurbita pepo (pumpkin) treatment.

Green and black tea extract blend

One RCT and 1 systematic review (current review), 1 RCT (2014 review) indicated that IPSS, peak urinary flow rate, and prostate volume were improved significantly with *Urtica dioica* than the placebo or controls.

Herbal remedies (*V. odorata* (sweet violet), *E. amoenum* (perennial herb) and *P. alkekengi* (Chinese lantern) *Urtica dioica* (extract from stinging nettle)

One RCT and 1 systematic review (current review) reported that IPSS improved following the treatments.

In summary, there is limited evidence on the efficacy of supplements for management of LUTS. Additional consistent conclusive evidence on the efficacy of selenium, silymarin, grape juice and soy isoflavones is needed before considering these for inclusion in the guideline.

Acupuncture

Laser acupuncture

Evidence from 2 studies at 2014 review and 3 RCTs from current review indicates that acupuncture may improve IPSS at short-term but no major effect after medium term follow-up. Therefore, the results of these studies are unlikely to change the direction of the current guideline recommendation which states that acupuncture should not be offered for treatment of LUTS in men.

Other alternative therapies

Biofeedback combined with physiokinesitherapy

The evidence from 1 RCT at 2014 review reported that preoperative biofeedback combined with an assisted low-intensity programme of postoperative perineal physiokinesitherapy may significantly improve incidence, duration and severity of urinary incontinence in patients undergoing radical prostatectomy.

No recommendations on biofeedback were made in the guideline and currently there is insufficient consistent conclusive new evidence to enable a recommendation to be made.

Tai chi (Chinese martial art)

Findings from an RCT in 2014 review showed that Tai chi may improve QoL in men with LUTS.

No recommendations on Chinese martial art were made in the guideline and currently there is insufficient consistent conclusive new evidence to enable a recommendation to be made.

Osteopathic treatment

An RCT identified at 2014 review found a significantly greater improvement in IPSS following osteopathic treatment compared to control. However, as no new evidence was found in current review, there is insufficient consistent conclusive new evidence to enable a recommendation to be made.

New evidence is unlikely to change guideline recommendations.

1.9 Providing information

Recommendations in this section of the guideline

- 1.9.1 Ensure that, if appropriate, men's carers are informed and involved in managing their LUTS and can give feedback on treatments.
- 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.
- 1.9.3 Provide men with storage LUTS (particularly incontinence) containment products at point of need, and advice about relevant support groups.

Surveillance proposal

These recommendations should not be updated.

Providing information

Self-management of LUTS

Previous surveillance summary

Findings from 1 RCT ([Yep et al. 2009](#)) at 2012 Evidence update and 1 RCT (373)

and 1 health economic evaluation (374) in 2014 surveillance reviews, showed that voiding behaviour of a self-management LUTS improved IPSS scores and QoL at 6 months follow-up compared with standard care. The economic evaluation reported that nurse specialist involvement for LUTS

was recommended as a suitable intervention for primary care.

2019 surveillance summary

No relevant evidence was identified.

Intelligence gathering

No relevant information was identified.

Impact statement

The evidence from 2 RCTs in previous reviews is in line with the current recommendation that supports self-management of LUTS.

New evidence is unlikely to change guideline recommendations.

Research recommendations

2.1 Multichannel cystometry

What is the clinical and cost effectiveness of multichannel cystometry in improving patient-related outcomes in men considering bladder outlet surgery?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance proposal

This research recommendation will be considered again at the next surveillance point.

2.2 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?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

2.3 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?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

2.4 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?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

2.5 Phosphodiesterase-5-inhibitors

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?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

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Appendix A: 2019 surveillance of Lower urinary tract symptoms in men: management (2010) NICE guideline CG97

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Appendix A: 2019 surveillance of Lower urinary tract symptoms in men: management (2010) NICE guideline CG97

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