NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Clinical Practice – Surveillance Programme

Clinical guideline
CG97: The management of lower urinary tract symptoms in men

Publication date
May 2010

Surveillance report for GE
July 2014

Key findings

	Potential impact on guidance	
	Yes	**No**
Evidence identified from Evidence Update		✓
Evidence identified from literature search	✓	
Feedback from Guideline Development Group	✓	
Anti-discrimination and equalities considerations		✓
Feedback from triage panel meeting	✓	

No update	GUC update	Standard update	Transfer to static list	Change review cycle
	✓			

Surveillance recommendation
GE is asked to consider the proposal to update the following clinical question in the guideline using the Standing Committee for Updates via the Clinical Guidelines Update Team:

- What is the clinical and cost-effectiveness of phosphodiesterase 5 inhibitor treatment of LUTS?

GE are asked to note that this 'yes to update' proposal will not be consulted on.

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Surveillance review of CG97: The management of lower urinary tract symptoms in men

Background information

Guideline issue date: 2010
4 year review: 2014

NCC: National Clinical Guidelines Centre

Triage panel recommendation

1. Through the 4 year surveillance review of CG97 new evidence (section 5) which may potentially impact guideline recommendations was identified in the following three clinical areas which were considered by the Triage Panel:

2. *What is the clinical and cost-effectiveness of phosphodiesterase 5 inhibitor treatment of LUTS?*
    a. The Triage Panel agreed that guidance on the use of phosphodiesterase 5 (PDE5) inhibitors, particularly tadalafil, is needed. The PDE5 inhibitor Tadalafil as monotherapy for the management of LUTS was covered by the terminated Technology Appraisal 273: Tadalafil for the treatment of symptoms associated with benign prostatic hyperplasia (Jan 2013). However, as TA273 has been terminated this drug could be included in an update of CG97 subject to GE approval.
    b. **Decision:** NICE to update this clinical question using Standing Committee for Updates via the Clinical Guidelines Update Team.

3. *What is the clinical and cost-effectiveness of combination therapy for treatment of LUTS?*
    a. The Triage Panel recognised that this question would need to be updated and suggested that the body of evidence on all combination options would need to be evaluated whilst a new economic evaluation would need to be carried out. However, the Triage Panel were aware of anticipated changes to drug costs over the next few years and queried whether it would be more

appropriate to defer the update to enable a new economic evaluation to be conducted once drugs have come off patent. Therefore, the Panel agreed to defer the update and wait for the results of the next surveillance review due in two years.

b. **Decision:** NICE to defer update of this clinical question.

4. *Intervention not currently included in the guideline - prostatic urethral lift for voiding symptoms*
    a. The Triage Panel indicated that the clinical efficacy evidence for this intervention is weak. As such, the group felt it was premature to initiate a standard update of the guideline and that deferring the update to the next surveillance review, to enable consideration of additional evidence in this area, would be more appropriate.
    b. **Decision:** NICE to defer update of this clinical question.

Outcome of four year surveillance review

5. The Evidence Update on CG97: LUTS (published March 2012) was used as a source of evidence for this surveillance review and considered new evidence since the guideline was published. No new evidence that would impact on the guideline recommendations was identified in the Evidence Update. An additional literature search for systematic reviews and RCTs was carried out between November 2011 (the end of the search period for the Evidence Update) and November 2013 and relevant abstracts were assessed. Clinical feedback on the guideline was obtained from six members of the GDG through a questionnaire.

6. New evidence that may impact on recommendations was identified relating to the following areas within the guideline:

Clinical area 1: Drug treatment – *recommendations 1.4.1 – 1.4.9*		
Q: What is the clinical and cost-effectiveness of combination therapy for treatment of LUTS?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence identified from literature search **Alpha blockers plus PDE5 inhibitor vs. alpha blocker** Four RCTs indicated that combination therapy of an alpha blocker and a PDE5 inhibitor improved LUTS compared with monotherapy with an alpha blocker.[1-4] Furthermore, one RCT reported no significant difference in treatment-emergent dizziness following administration of combination therapy compared with placebo.[5] Conversely, one RCT which compared the efficacy of alfuzosin	Feedback from the GDG indicated that new evidence has emerged relating to PDE5 inhibitors for LUTS which may impact on the guideline.	The identified new evidence indicated improvement in LUTS following combination therapy with an alpha blocker and a PDE5 inhibitor compared with alpha blocker monotherapy. Similar results were obtained in studies which compared combination therapy with PDE5 inhibitor monotherapy. This differs from the evidence included in the guideline which found no significant difference between

alone or in combination with sildenafil in the treatment of LUTS due to benign prostatic hyperplasia indicated that combination therapy did not have a better efficacy than alpha blocker treatment alone.[6] **Alpha blockers plus PDE5 inhibitor vs. PDE5 inhibitor** One RCT[7] and a systematic review[8] reported that alpha blocker plus PDE5 inhibitor combination therapy significantly improved International Index of Erectile Function (IIEF-5), International Prostate Symptom Score (IPSS) score and maximum urinary flow rate (Qmax) compared with PDE5 inhibitor monotherapy.		combination treatment of alpha blockers plus PDE5 inhibitors versus alpha blockers (3 RCTs) or PDE5 inhibitors (2 RCTs) in improving symptom scores, quality of life (IPSS question), nocturia or frequency at up to 3 months follow-up. No recommendations on combination therapy with alpha blockers and PDE5 inhibitors are included in the guideline although the GDG provided a research question on the clinical and cost effectiveness of PDE5 inhibitor and PDE5 inhibitor/alpha blocker combinations compared to placebo in men with LUTS. There is a now a body of evidence suggesting that this combination treatment strategy may be more effective than monotherapy and may enable a recommendation to be made. The PDE5 inhibitor Tadalafil as monotherapy for the management of LUTS has been covered by the terminated Technology Appraisal 273: Tadalafil for the treatment of symptoms associated with benign prostatic hyperplasia (Jan 2013). As TA273 has been terminated, this drug could be included in an update of CG97 subject to GE approval.
Q: What is the clinical and cost-effectiveness of phosphodiesterase 5 inhibitor treatment of LUTS?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence identified from literature search A body of evidence was identified which indicated that PDE5 inhibitors may improve LUTS symptoms and may represent an	The GDG highlighted that PDE5 inhibitors have now been licensed for LUTS.	The guideline does not currently include any recommendations on PDE5 inhibitors. The PDE5 inhibitor Tadalafil as monotherapy for

alternative to current treatments of men with LUTS.[9-19] Four RCTs[9,14,19,20], one meta-analysis[10] and two post-hoc analyses[15,16] indicated that tadalafil significantly improved lower urinary tract symptoms compared with placebo. Furthermore, one RCT found improvement in maximal flow and average flow (Qmax and Qave) in men following treatment with sildenafil citrate compared with placebo.[18] One RCT comparing tadalafil with solifenacin (an antimuscarinic) for persistent storage symptoms after prostate surgery observed a significant and comparable improvement of urinary symptoms with a decrease of IPSS value in both groups.[13] Two studies comparing doses of tadalafil found more improvement with a 5mg dose compared with 2.5mg.[11,17]		the management of LUTS was covered by the terminated Technology Appraisal 273: Tadalafil for the treatment of symptoms associated with benign prostatic hyperplasia (Jan 2013). However, as TA273 has been terminated this drug could be included in an update of CG97 subject to GE approval. Tadalafil for benign prostatic hyperplasia was evaluated 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) although this does not constitute NICE guidance. This Evidance Sumary highlights that prescribing of tadalafil for erectile dysfunction in England is subject to statutory prescribing restrictions however, these prescribing restrictions do not apply to tadalafil when it is prescribed in primary care on the NHS for benign prostatic hyperplasia (Department of Health: personal communication October 2013). There is now a body of evidence comparing PDE5 inhibitors with placebo which is relevant to the research recommendation in the guideline: what is the clinical and cost effectiveness of PDE5I and PDE5I/alpha blocker combinations compared to placebo in

		men with LUTS? The results of these trials may enable a recommendation to be made about PDE5 inhibitors for treatment of LUTS.
Clinical area 2: Surgery for voiding symptoms		
Intervention not currently included in the guideline - prostatic urethral lift		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence identified from literature search Two RCTs comparing prostatic urethral lift with sham for treatment of LUTS reported improvement in symptoms from baseline up to 12 months[21,22]. This intervention has been covered in a related Interventional Procedure IPG475: Insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia (published January 2014). The Interventional Procedure guidance recommended 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 provided that normal arrangements are in place for clinical governance, consent and audit.	Feedback from the GDG indicated that an RCT on the prostatic urethral lift procedure has published.	Prostatic urethral lift is an intervention not currently covered by the guideline. This is potentially a new intervention that could be considered alongside the other management options for benign prostatic hyperplasia secondary to LUTS.

Ongoing research

7. None identified.

Anti-discrimination and equalities considerations

8. None identified.

Implications for other NICE programmes

9. This guideline relates to a Quality Standard on Lower urinary tract symptoms (QS45 published September 2013).

10. None of the quality statements are likely to be affected by the proposed areas for update.

Conclusion

11. Through the review of CG97 new evidence which may potentially impact guideline recommendations was identified in the following areas and discussed at the Triage Panel meeting:
    a. The clinical effectiveness of PDE5 inhibitor monotherapy for treatment of LUTS
    b. The clinical effectiveness of alpha blockers plus PDE5 inhibitor combination therapy for treatment of LUTS
    c. Prostatic urethral lift as a new management option for benign prostatic hyperplasia secondary to LUTS

12. For all other areas of the guideline no evidence was identified which would impact on recommendations.

Surveillance recommendation (post Triage Panel)

13. GE is asked to consider the proposal to update the following question in the guideline using Standing Committee for Updates via Clinical Guidelines Update Team:
    a. What is the clinical and cost-effectiveness of phosphodiesterase 5 inhibitor treatment of LUTS?

14. GE are asked to note that this 'yes to update' proposal will not be consulted on.

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Centre for Clinical Practice
July 2014

Appendix 1 Decision matrix

Surveillance and identification of triggers for updating CG97. The table below provides summaries of the evidence for key questions for which studies were identified.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
What is the sensitivity and specificity of urinalysis to detect each relevant condition (diabetes, bladder cancer, urinary tract infections, stones, renal disease)?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
How does baseline PSA predict symptom progression?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
In men with LUTS, does performing a PSA test affect patient outcomes versus not performing the diagnostic test?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
In men with LUTS, does completing symptom scores affect patient outcomes (including futile treatment and missed treatment opportunities) versus not completing scores?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
In men with LUTS, what is the effectiveness of a DRE versus no DRE in changes to patient treatment/outcomes?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
In men with LUTS, what is the effectiveness of frequency volume chart versus no frequency volume chart in changes to patient treatment/outcomes?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
In men with LUTS how does measuring incontinence (pad test) affect patient outcomes versus not performing the diagnostic test?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
In men with LUTS how does measuring renal function affect patient outcomes versus not performing the diagnostic test?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
In men with LUTS, what is the effectiveness of urinary flow rate versus no urinary flow rate in relationship to patient treatment/outcomes?			

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
No new key evidence was found for this section.	One study was identified which investigated the accuracy of uroflowmetry with disposable Q Single compared to measurements with a home-based digital device or clinic-based method in men with LUTS.[23] Mean Q max obtained with the Q(Single) device did not differ from that obtained with the clinic method whilst mean voided volumes recorded with each device differed marginally. However, this study did not compare the use of uroflowmetry with no uroflowmetry and is unlikely to impact the guideline recommendations which do not currently specify how measurement of flow rate should be conducted.	None identified.	New evidence is unlikely to impact on guideline recommendations.
What is the sensitivity and specificity of a maximum urinary flow rate in predicting bladder outlet obstruction as defined by pressure flow studies in men with LUTS?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
In men with LUTS, what is the effectiveness of post void residual measurement versus no post void residual measurement in relationship to patient treatment/outcomes?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
What is the sensitivity and specificity of post void residual measurement in predicting urodynamic diagnosis as defined by pressure flow studies in men with LUTS?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
In men with LUTS, what is the effectiveness of performing multichannel cystometry tests versus not performing the diagnostic test?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
In men with LUTS how does performing cystoscopy affect patient outcomes versus not performing the diagnostic test?			
No new key evidence was found for this section.	One study conducted in patients presenting with haematuria who underwent cystoscopy as part of their	The GDG highlighted that HTA trials will soon be	New evidence is unlikely to impact on guideline

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	evaluation found that this method accurately stratified patients with high confidence into those who were likely to have or not have bladder cancer.[24] Cystoscopy is currently recommended in men with LUTS if they have a history of haematuria therefore, this new evidence is unlikely to change the direction of the guideline recommendations.	commencing with the aim of evaluating the diagnostic value of preoperative urodynamics in men with LUTS.	recommendations.
In men with LUTS how does performing imaging (transabdominal ultrasound, intravenous urogram or plain abdominal x-ray) affect patient outcomes versus not performing the diagnostic test?			
No new key evidence was found for this section.	The utility of prostate ultrasound in the diagnosis of infravesical obstruction (IVO) and detrusor hyperactivity (DH) was assessed in one study.[25] Abdominal ultrasound was used to calculate detrusor thickness/weight, prostate volume, and middle lobe length. The results indicated that ultrasound had high sensitivity and specificity for diagnosing IVO but not DH. A second study concluded that suprapubic transabdominal ultrasonographic assessment of the lower urinary tract enabled noninvasive assessment of LUTS.[26] Currently imaging of the upper urinary tract is only recommended for men with LUTS having specialist assessment and only when clinically indicated but no specific imaging modality is recommended. Neither study reported on the risks associated with the investigations nor the costs of the imaging procedures assessed which was a major consideration by the GDG. As such, this new evidence is unlikely to impact on the guideline recommendation.	None identified.	New evidence is unlikely to impact on guideline recommendations.
In men who report LUTS, what is the effect of pelvic floor muscle training versus any other conservative therapy or no treatment on patient related and biometric outcomes and adverse events?			

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
No new key evidence was found for this section.	Five RCTs and 3 systematic reviews were identified which evaluated the impact of pelvic floor muscle training for LUTS. One RCT compared the efficacy of preoperative pelvic floor muscle training with pelvic floor muscle training after catheter removal following surgery in patients undergoing radical prostatectomy.[27] Patients with additional preoperative pelvic floor muscle training had no shorter duration of postoperative urinary incontinence compared with patients with only postoperative pelvic floor muscle training. Two RCTs compared pelvic floor muscle training with electrical stimulation and biofeedback. One RCT[28] reported significantly lower leakage weight in the electrical stimulation plus biofeedback group compared with pelvic floor muscle training whilst the second study[29] found no improvement in adding biofeedback or electrical stimulation to pelvic floor muscle training. One Cochrane systematic review found an overall benefit from pelvic floor muscle training versus control management in terms of reduction of urinary incontinence.[30] In addition, one RCT observed a decrease in the IPSS among men who performed daily pelvic floor muscle exercises following transurethral resection of the prostate compared with control.[31] Improvement in postoperative urinary incontinence was observed in men carrying out physiotherapist-guided pelvic floor muscle training compared with self-training following radical prostatectomy.[32] Conversely,	None identified.	New evidence is unlikely to impact on guideline recommendations.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	a report of two RCTs found that the rate of urinary incontinence following formal one-to-one pelvic floor muscle training in men following radical prostatectomy at 12 months was not significantly different from the control group.[33] Similarly, an HTA concluded that the provision of one-to-one conservative physical therapy for men with urinary incontinence after prostate surgery was neither effective or cost-effective compared with standard care.[34] The evidence on pelvic floor muscle training was heterogeneous, conducted in different populations and utilising different protocols for treatment. Supervised pelvic floor muscle training is currently recommended for men with stress urinary incontinence caused by prostatectomy and there is no consistent new evidence which would change the direction of this recommendation.		
In men who report LUTS, what is the effect of biofeedback versus any other conservative therapy or no treatment on patient related and biometric outcomes and adverse events?			
No new key evidence was found for this section.	One RCT reported that preoperative biofeedback combined with an assisted low-intensity programme of postoperative perineal physiokinesitherapy was significantly better than control in reducing the incidence, duration and severity of urinary incontinence in patients undergoing radical prostatectomy.[35] 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.	None identified.	Insufficient consistent conclusive evidence to enable a recommendation to be made.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
In men who report LUTS, what is the effect of electrical stimulation versus any other conservative therapy or no treatment on patient related and biometric outcomes and adverse events?			
No new key evidence was found for this section.	Two systematic reviews on electrical stimulation for urinary incontinence were identified. The results were mixed with one review[36] reporting that electrical stimulation did not improve recovery of urinary incontinence better than pelvic floor muscle training whilst the second review[37] 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. However, the same review also reported that there was no evidence of a statistically significant difference in the number of men with urinary incontinence at three months for electrical stimulation plus pelvic floor muscle training versus pelvic floor muscle training alone. No recommendations on electrical stimulation were made in the guideline and currently there is insufficient consistent conclusive new evidence to enable a recommendation to be made.	None identified.	Insufficient consistent conclusive evidence to enable a recommendation to be made.
In men who report LUTS, what is the effect of bladder training versus any other conservative therapy or no treatment on patient related and biometric outcomes and adverse events?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
In men who report LUTS, what is the effect of post void milking versus any other conservative therapy or no treatment on patient related and biometric outcomes and adverse events?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
In men who report LUTS, what is the effect of timing of fluid intake versus no change in timing of fluid intake or any other conservative therapy on patient related and biometric outcomes and adverse events?			
No new key evidence was found for	No studies identified.	None identified.	No relevant evidence

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
this section.			identified.
In men who report LUTS, what is the effect of reducing alcohol/caffeine/artificial sweeteners/carbonated drink intake versus no reduction in their intake or any other conservative therapy on patient related and biometric outcomes and adverse events?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
In men who report LUTS, what is the effect of one type of product (pads, pants, bedpants, penile sheaths appliances and penile clamps) versus no product or other conservative therapy on patient related and biometric outcomes and adverse events?			
The Evidence Update included a crossover RCT by Chartier-Kastler et al. (2010) and concluded that this study had no impact on the guideline, which recommends either sheaths or pads, because this study only provides some evidence that one particular sheath device has some QoL benefit over incontinence pads.	One RCT compared urisheaths with absorbent products in men with moderate to severe urinary incontinence.[38] All dimensions of the King's Health Questionnaire were scored lower with urisheaths, indicating an improvement in QoL. The majority of patients preferred Conveen Optima urisheaths to their usual absorbent products. The results of this study are unlikely to impact the current recommendation which states that men with LUTS should be offered a choice of containment products based on individual circumstances.	None identified.	New evidence is unlikely to impact on guideline recommendations.
In men who report LUTS, what is the effect of intermittent catheters compared to indwelling catheters on patient related and biometric outcomes and adverse events?			
No new key evidence was found for this section.	In summary, two systematic reviews on catheterisation were identified. Minor complications following catheterisation, including urine leakage, were reported in one systematic review.[39] This supports the recommendation that men should be informed of the risks of catheterisation. Lastly, one systematic review indicated that a hydrogel coated latex catheter rather than a silicone catheter	None identified.	New evidence is unlikely to impact on guideline recommendations.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	may be better tolerated.[40] 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.		
What is the clinical and cost-effectiveness of alpha blocker treatment of LUTS?			
Silodosin The Evidence Update included a study by Chapple et al. (2011) which evaluated the superiority of silodosin over placebo and non-inferiority to tamsulosin in the treatment of LUTS. The EUAG concluded that silodosin has efficacy comparable to, but without additional benefits over, tamsulosin however, these results would not affect recommendations in the guideline, because silodosin is not available in the UK. *Naftopidil* A Cochrane review by Garimella et al. (2009) evaluated the efficacy and safety of naftopidil for the treatment of LUTS associated with BPH. Naftopidil achieved similar effects to tamsulosin in all variables evaluated. However, the Evidence Update concluded that the evidence on naftopidil would not affect recommendations in CG97	*Alfuzosin* One cross-over RCT compared the efficacy and safety of alfuzosin and tamsulosin in patients with LUTS associated with BPH.[41] In the first treatment period, each drug significantly improved IPSS and Q max whilst cross-over was also effective in improving IPSS and Q max. This new evidence is unlikely to impact the guideline recommendations as both alfuzosin and tamsulosin are already recommended for men with moderate to severe LUTS. *Tamsulosin* Two systematic reviews[42,43] and three RCTs[44-46] reported that tamsulosin improved lower urinary tract symptoms compared with placebo. One small-scale RCT compared tamsulosin with herbal medicines (extracts of Murraya koenigii and Tribulus terrestris leaves) in men with BPH.[47] No significant difference between groups for IPSS score was observed. Lastly, one RCT evaluated the efficacy and safety of tamsulosin 0.4mg once daily verses finasteride in men with symptomatic BPH.[48] The results indicated that both drugs reduced the total and individual I-PSS scores, while tamsulosin significantly improved lower	None identified.	New evidence is unlikely to impact on guideline recommendations.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
because this drug is not licensed in the UK.	urinary tract symptoms compared to finasteride within 3-months of therapy. This new evidence is unlikely to impact the guideline recommendations as tamsulosin is already recommended for men with moderate to severe LUTS. *Silodosin* The results of three systematic reviews[49-51], an RCT[52], a post-hoc analysis of an RCT[53] and a pooled analysis of two RCTs[54] indicated that silodosin achieved significant improvement in LUTS compared with placebo. Four studies reported that silodosin had similar efficacy to tamsulosin.[50,51,55,56] Additionally, the results of one crossover RCT comparing the efficacy and safety of tamsulosin and silodosin in the treatment of male LUTS found that symptoms improved in both groups with no significant differences between the groups.[57] Lastly, one RCT compared the efficacy of Silodosin versus naftopidil for LUTS associated with BPH.[58] The results indicated that silodosin and naftopidil significantly improved the total IPSS and QoL however, silodosin obtained significantly better improvement in total IPSS in alpha-blocker-naive patients at 4 and 8 weeks. Silodosin is not currently licensed for use in the UK therefore, it would be pertinent to wait for this treatment to be granted a UK license and to await further evidence, particularly on the benefits, harms and cost-effectiveness, before an update of this review question is commissioned.		

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	Doxazosin Two RCTs compared the doxazosin gastrointestinal therapeutic system (doxazosin-GITS) and tamsulosin in men with LUTS suggestive of BPH.[59,60] An improvement in symptom scores was observed for both treatments although significantly greater improvements in some outcomes were observed in one of the studies for the doxazosin-GITS group. Both doxazosin and tamsulosin are recommended for use in men with moderate to severe LUTS and the guideline indicates that the choice is often patient led. As such, this new evidence is unlikely to impact on the current recommendation. *Terazosin* One systematic review evaluated the effectiveness and adverse effects of terazosin for treatment of urinary symptoms associated with benign prostatic obstruction (BPO).[61] The results indicated that terazosin improved urinary symptoms and flow measures associated with BPO with an effect similar to other alpha-blockers. This new evidence is unlikely to impact the guideline recommendations as terazosin is already recommended for men with moderate to severe LUTS.		
What is the clinical and cost-effectiveness of 5α-reductase inhibitor treatment of LUTS?			
General The Evidence Update reported that the US Food and Drug Administration has issued safety advice for 5-alpha reductase inhibitors recommending	A systematic review for treatment of symptomatic benign prostatic hyperplasia indicated that dutasteride is an effective, safe and well-tolerated treatment either as monotherapy or in combination with an alpha-blocker.[62] In addition, a meta-analysis[63] found that	None identified.	New evidence is unlikely to impact on guideline recommendations.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
that urological conditions that mimic BPH (such as prostate cancer) should be ruled out before starting treatment with drugs from this class. *Dutasteride plus testosterone* A double-blind, single centre RCT by Page et al. (2011) compared changes in prostate size, prostate-specific antigen (PSA) and androgen levels (primary outcomes) after 6 months of treatment with testosterone plus dutasteride compared with testosterone alone. The Evidence Update concluded that this study was small and had a short follow-up so was not likely to affect recommendations in the guideline. However, the study provided some evidence that dutasteride plus testosterone leads to improvement in biological outcomes. *Finasteride* A Cochrane review undertaken by Tacklind et al. (2010) compared the clinical effectiveness and side effects of finasteride versus placebo and active controls in the treatment of LUTS. Finasteride consistently improved urinary symptom scores more than placebo in trials of more than 1 year in duration. The Evidence	dutasteride was not associated with a statistically significant increased risk of heart failure, myocardial infarction and stroke compared to controls whilst a post-hoc analysis of a trial reported that dutasteride significantly reduced clinical progression of BPH.[64] Compared with placebo, dutasteride improved Qmax and American Urology Association Symptom Index at 3 and 6 months in men with BPH.[65] One RCT compared of dutasteride with finasteride in men with BPH reporting that both treatments were effective at reducing prostate volume with no significant difference between the two treatments during the study.[66] In addition, two studies comparing finasteride with placebo for BPH found the treatment to be cost-effective[67] and to have a significant beneficial effect on clinical progression[68]. 5-alpha reductase inhibitors are recommended for 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). From an assessment of abstracts it was not specified if the included population had prostates larger than 30 g or high PSA levels however, the identified new evidence on dutasteride and finasteride indicated these treatments have efficacy in men with BPH and is therefore unlikely to impact on the guideline recommendation.		

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
Update concluded that this review supports the guideline which recommends treatment with alpha blockers for moderate to severe LUTS. *Dutasteride versus finasteride* One RCT (the Enlarged Prostate International Comparator study; EPICS) compared the efficacy and safety of dutasteride and finasteride in the treatment of men (aged ≥ 50 years) with symptomatic BPH (Nickel et al. 2011). The Evidence Update concluded that as the study found both 5-alpha reductase inhibitors were equally effective treatments for LUTS this reinforces current clinical practice and recommendations in NICE GC97, which does not indicate a preferred drug in this class.			
What is the clinical and cost-effectiveness of anticholinergic treatment of LUTS?			
A systematic review by Athanasopoulos et al. (2011) assessed the efficacy of drugs (previously known as anticholinergics) for LUTS. The Evidence Update concluded that the review supports the recommendations in the guideline which suggest offering antimuscarinics (referred to as anticholinergics in the guideline) to men with OAB, and combination	*General* One systematic review reported that combined antimuscarinic+ alpha-blocker treatment is generally more effective than monotherapy or placebo in men with overactive bladder.[69] Post hoc analyses from placebo-controlled trials also suggest that antimuscarinics are generally safe and efficacious in men. In addition, a second systematic review found that in a comparison between solifenacin and immediate release tolterodine, solifenacin had better	The GDG highlighted that mirabegron is now available which is an alternative to anticholinergics. However, this drug therapy has been covered in a related Technology Appraisal: TA290 Overactive bladder – mirabegron (published June 2013).	The identified new evidence is unlikely to change the direction of the guideline recommendation which states that men should be offered an anticholinergic to manage the symptoms of overactive bladder.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
treatment with alpha-blockers and antimuscarinics for those with persisting storage symptoms.	efficacy and less risk of dry mouth whilst fesoterodine demonstrated superior efficacy compared to tolterodine but had a higher risk of withdrawal due to adverse events and higher risk of dry mouth.[70] The identified new evidence is unlikely to change the direction of the guideline recommendation which states that men should be offered an anticholinergic to manage the symptoms of overactive bladder. *Fesoterodine* An economic analysis found that treatment with fesoterodine resulted in similar overall costs and greater QALY gain than treatment with either tolterodine or solifenacin.[71] The results of five RCTs indicated that fesoterodine was associated with greater improvements in lower urinary tract symptoms compared with placebo.[72-76] The efficacy and tolerability of fesoterodine versus tolterodine extended release (ER) in subjects with overactive bladder was assessed in a post-hoc analysis of data from two double-blind trials.[77] Symptom improvement was significantly greater with fesoterodine versus tolterodine ER. A pooled analysis of two identically designed open-label extensions of 12-week RCTs of fesoterodine in patients with overactive bladder was identified which indicated that long-term fesoterodine was well tolerated and associated with sustained improvements in overactive bladder symptoms.[78] The identified new evidence is unlikely to change the direction of the guideline recommendation which states that men should be offered an anticholinergic to manage the symptoms of overactive bladder.	Furthermore, the GDG indicated that anticholinergics are now referred to as antimuscarinics which may cause confusion for clinicians when prescribing treatment.	However, reference to anticholinergics in the guideline and recommendations could be refreshed to take into consideration the change in name to antimuscarinics.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	Solifenacin One RCT was identified which determined the efficacy of 5 and 10 mg solifenacin doses in relieving overactive bladder symptoms.[79] Greater reductions in the mean number of severe urgency episodes were observed from week 8 to the end of treatment for patients randomised to 10 mg solifenacin compared with those randomised to remain on 5 mg, although these did not reach statistical significance. Furthermore, one RCT compared the incidence and severity of dry mouth and other adverse events with solifenacin 5 mg/day and oxybutynin immediate release (IR) 15 mg/day in patients with overactive bladder.[80] Solifenacin 5 mg/day was associated with fewer episodes and lower severity of dry mouth, and a lower discontinuation rate, compared with oxybutynin IR 15 mg/day. The identified new evidence is unlikely to change the direction of the guideline recommendation which states that men should be offered an anticholinergic to manage the symptoms of overactive bladder. *Propiverine* The efficacy and safety of propiverine versus placebo for overactive bladder was assessed in an RCT.[81] Compared to placebo, propiverine produced significant improvements in urgency, urgency incontinence, urine volume/micturition, and the overactive bladder symptom score. The identified new evidence is unlikely to change the direction of the guideline recommendation which states that men should be		

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	offered an anticholinergic to manage the symptoms of overactive bladder. *Oxybutynin* A cost-effectiveness analysis of anti-muscarinic agents for the treatment of overactive bladder indicated a broad overlap in effectiveness among anti-muscarinic agents, except solifenacin had a significantly higher continence rate.[82] Oxybutynin IR and oxybutynin ER were significantly less costly than other anti-muscarinic regimens. The identified new evidence is unlikely to change the direction of the guideline recommendation which states that men should be offered an anticholinergic to manage the symptoms of overactive bladder. *Trospium chloride* Two studies assessing the efficacy and safety of trospium chloride for overactive bladder reported significantly greater decreases from baseline in the mean number of daily toilet voids and urgency urinary incontinence episodes in men at week 12 versus placebo[83] and no difference compared with placebo for treatment-emergent adverse events[84]. The identified new evidence is unlikely to change the direction of the guideline recommendation which states that men should be offered an anticholinergic to manage the symptoms of overactive bladder.		
What is the clinical and cost-effectiveness of phosphodiesterase 5 inhibitor treatment of LUTS?			
The Evidence Update indicated that tadalafil for the treatment of BPH has	A systematic review was identified which suggested that PDE5-Is might represent an alternative to current	The GDG highlighted that PDE5 inhibitors have now	The guideline does not currently include any

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
been proposed for consideration in a NICE technology appraisal. A decision on inclusion in NICE's work programme was expected by April 2012.	treatments of men with LUTS.[12] Four RCTs[9,14,19,20], one meta-analysis[10] and two post-hoc analyses[15,16] indicated that tadalafil significantly improved lower urinary tract symptoms compared with placebo. Furthermore, one RCT found improvement in maximal flow and average flow (Qmax and Qave) in men following treatment with sildenafil citrate compared with placebo.[18] One RCT comparing tadalafil with solifenacin for persistent storage symptoms after prostate surgery observed a significant and comparable improvement of urinary symptoms with a decrease of IPSS value in both groups.[13] Two studies comparing doses of tadalafil found more improvement with a 5mg dose compared with 2.5mg.[11,17] The guideline does not currently include any recommendations on PDE5 inhibitors however tadalafil for benign prostatic hyperplasia was 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)..	been licensed for LUTS.	recommendations on PDE5 inhibitors. The PDE5 inhibitor Tadalafil as monotherapy for the management of LUTS was covered by the terminated Technology Appraisal 273: Tadalafil for the treatment of symptoms associated with benign prostatic hyperplasia (Jan 2013). However, as TA273 has been terminated this drug could be included in an update of CG97 subject to GE approval. Tadalafil for benign prostatic hyperplasia was 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) although this does

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
			not constitute NICE guidance. There is now a body of evidence comparing PDE5 inhibitors with placebo which is relevant to the research recommendation in the guideline: what is the clinical and cost cost effectiveness of PDE5I and PDE5I/alpha blocker combinations compared to placebo in men with LUTS? The results of these trials may enable a recommendation to be made about PDE5 inhibitors for treatement of LUTS.
What is the clinical and cost-effectiveness of diuretics for treatment of LUTS?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
What is the clinical and cost-effectiveness of desmopressin for treatment of LUTS?			
A placebo-controlled RCT by Wang et al. (2011) evaluated the long-term efficacy and safety of low dose desmopressin at bedtime in men aged ≥ 65 years with BPH. The Evidence Update concluded that the study supports the recommendations in the	Two RCTs comparing the efficacy of desmopressin with placebo in men with BPH and nocturia reported significantly decreased nightly voids following treatment with desmopressin.[85,86] Lastly, one RCT which compared desmopressin and doxazosin in patients with nocturia and BPH observed improvements in symptoms with a significant	None identified.	New evidence is consistent with guideline recommendations.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
guideline, which suggest using desmopressin for nocturnal polyuria if other medical causes have been excluded and other treatments have not worked.	difference between groups for IPSS but not number of nocturia, residual urine volume, quality of life scores and peak urinary flow rates.[87] 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.		
What is the clinical and cost-effectiveness of non-steroidal anti-inflammatory drugs for treatment of LUTS?			
No new key evidence was found for this section.	A systematic review and meta-analysis was identified which evaluated the safety and long-term impact of NSAID use in men with BPH.[88] The results indicated that NSAIDs improved urinary symptom scores and flow measures. 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 to placebo in reducing symptom progression for men with lower urinary tract symptoms but further evidence is required on costs and long-term safety and efficacy.	None identified.	Insufficient consistent conclusive evidence to enable a recommendation to be made.
What is the clinical and cost-effectiveness of combination therapy for treatment of LUTS?			
Alpha blockers plus 5-alpha reductase inhibitors (5-ARI) vs. 5-alpha reductase inhibitors or alpha blockers One RCT (the Combination of Avodart and Tamsulosin [CombAT] study) by Roehrborn et al. (2010) assessed whether dutasteride and tamsulosin combination therapy is more effective than either drug as monotherapy in	***Combination therapy (alpha blockers plus 5-alpha reductase inhibitors)*** ***Alpha blocker plus 5-alpha reductase inhibitor vs. alpha blocker*** *Tamsulosin and dutasteride vs. tamsulosin* Five studies (RCTs and post-hoc analyses) concluded that the evidence supports the efficacy and safety of	None identified.	**Combination therapy (alpha blockers plus PDE5 inhibitor)** No recommendations on combination therapy with alpha blockers and PDE5 inhibitors are included in the guideline although the GDG provided a research

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
increasing the time to acute urinary retention or BPH-related surgery over 4 years. The Evidence Update concluded that as the study looked at men with large prostates (≥ 30 cm^3) and found efficacy for combination therapy, this data reinforce the recommendation in CG97 that combination therapy can be considered for men with large prostates. <u>Alpha blocker plus antimuscarinic vs. alphablocker</u> A large multicentre double-blind RCT by Yamaguchi et al. (2011) evaluated the effects of solifenacin as an additional treatment for men with LUTS who were also receiving treatment with tamsulosin. The combination group had significantly greater improvements in urinary symptoms compared with monotherapy. A such, the Evidence Update concluded that the results of this study reinforces current recommendations to consider combination therapy for men who still have symptoms after treatment with an alpha blocker.	tamsulosin in combination with dutasteride compared with monotherapy in treating men with LUTS.[89-93] Furthermore, a post-hoc analysis of the CombAT study indicated that the benefit of combination therapy over dutasteride was confined to groups with lower baseline prostate volume (<60 cc) and PSA (<4 ng/ml).[94] *Alpha-blocker and 5-alpha reductase inhibitor vs. alpha blocker* One RCT compared alpha-blocker monotherapy with combination therapy involving an alpha-blocker and a 5-alpha reductase inhibitor for BPH.[95] Combination therapy resulted in significant improvements in prostate volume, IPSS and Q max, which were most pronounced in men with a prostate volume > 35 ml. Furthermore, one systematic review assessed the efficacy and adverse events of alpha blocker/5alpha-reductase inhibitor combination therapy for male LUTS.[96] The combination therapy appeared to be more efficacious in patients whose prostate volume was between 30 ml and 40 ml and treatment was maintained for >1 yr. However, when treatment was given for <1 yr, alpha blockers alone were just as effective. *Doxazosin and finasteride vs. doxazosin* One RCT examined the effects of doxazosin, finasteride and combination therapy among men with BPH.[97] Compared with men assigned to placebo, men assigned to doxazosin and combination experienced a significant improvement in I-PSS-QoL and the BII at		question on the clinical and cost effectiveness of PDE5I and PDE5I/alpha blocker combinations compared to placebo in men with LUTS. There is a now a body of evidence suggesting that this combination treatment strategy may be more effective than monotherapy and may enable a recommendation to be made. The PDE5 inhibitor Tadalafil for the management of LUTS has been covered by the terminated Technology Appraisal 273: Tadalafil for the treatment of symptoms associated with benign prostatic hyperplasia (Jan 2013). As TA273 has been terminated, this drug could be included in an update of CG97 subject to GE approval.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	year 4. In summary, the identified new evidence indicates that alpha blocker plus 5-alpha reductase inhibitor combination therapy has a beneficial effect on LUTS compared with monotherapy. A combination of an alpha blocker and a 5-alpha reductase inhibitor is recommended for men with bothersome moderate to severe LUTS and no new evidence was identified which would change the direction of this recommendation. ***Combination therapy (alpha blockers plus PDE5 inhibitor)*** **Alpha blockers plus PDE5 inhibitor vs. alpha blocker** *Tamsulosin and vardenafil vs. tamsulosin* One RCT compared the safety and efficacy of tamsulosin vs. tamsulosin plus vardenafil in patients with LUTS/BPH.[8] Combination treatment for 12 weeks was well tolerated and more effective in improving LUTS and erectile function, as compared with tamsulosin alone. *Alpha-blockers and tadalafil vs. placebo* One RCT assessed the efficacy and safety of daily coadministration of alpha-blockers with tadalafil in men with LUTS secondary to BPH reporting no significant difference in treatment-emergent dizziness was observed following administration of combination		

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	therapy compared with placebo.[5] *Tamsulosin and tadalafil vs. tamsulosin* One RCT compared tamsulosin and tadalafil with tamsulosin and placebo in men with LUTS.[3] Total IPSS, storage, and voiding sub-score improved significantly in the combination group compared with the tamsulosin/placebo group. The results of a second RCT indicated that tamsulosin and tadalafil alone or in combination cause a significant improvement in patients with LUTS.[4] *Tadalafil and standard medication (not specified in study abstract)* One RCT evaluated the safety and efficacy of tadalafil combined with standard medication on LUTS suggestive of BPH[2] Tadalafil as an add-on to standard medication improved quality of life and urinary symptoms but did not have any significant effect on Qmax. *Alfuzosin and sildenafil vs. alfuzosin* One RCT which compared the efficacy of alfuzosin alone or in combination with sildenafil in the treatment of LUTS due to BPH indicated that combination therapy did not have a better efficacy than alpha blocker treatment alone.[6] **Alpha blockers plus PDE5 inhibitor vs. PDE5 inhibitor** *Doxazosin and sildenafil vs. sildenafil*		

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	One RCT evaluated the clinical efficacy and safety of combined oral therapy with sildenafil and doxazosin GITS compared to sildenafil monotherapy in treating men with LUTS secondary to BPH.[7] After treatment, IIEF-5, IPSS and QoL scores were significantly improved in the combination group. *PDE5-Is and alpha blockers vs. PDE5-Is or alpha blocker monotherapy* A systematic review evaluated the use of PDE5-Is alone or in combination with alpha blockers in patients with LUTS/BPH concluding that combination therapy improved the IIEF score, IPSS score, and Qmax at the end of the study as compared with monotherapy.[8] The identified new evidence indicated improvement in LUTS following combination therapy with an alpha blocker and a PDE5 inhibitor compared with alpha blocker monotherapy. Similar results were obtained in studies which compared combination therapy with PDE5 inhibitor monotherapy. This differs from the evidence included in the guideline which found no significant difference between combination treatment of alpha blockers plus PDE5 inhibitors and alpha blockers or PDE5 inhibitors in improving symptom scores, quality of life (IPSS question), nocturia or frequency at up to 3 months follow-up. No recommendations on combination therapy with alpha blockers and PDE5 inhibitors are included in the guideline although the GDG provided a research question on the clinical and cost effectiveness of PDE5I and PDE5I/alpha blocker combinations		

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	compared to placebo in men with LUTS. There is a now a body of evidence suggesting that this combination treatment strategy may be more effective than monotherapy and may enable a recommendation to be made. ***<u>Combination therapy (antimuscarinic plus alpha blockers)</u>*** ***Antimuscarinic plus alpha blocker vs. alpha blocker*** *Trospium chloride and terazosin vs. terazosin and placebo* One RCT evaluated the efficacy and safety of trospium chloride plus terazosin versus placebo plus terazosin in men with BPH-related LUTS with overactive bladder[98] Improvement in maximum and average urination streams, bladder capacity and IPSS was not significant. However, there was significant improvement in voiding frequency in favour of the combination group. *Propiverine and terazosine vs. terazosine and placebo* One RCT investigated the long term efficacy and safety of the use of propiverine and terazosine combination compared with terazosine plus placebo in patients with LUTS and detrusor overactivity.[99] After one year of treatment, there was significant improvement in IPSS, IPSS4, OAB symptoms, QoL and Qmax values in the combination group.		

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	Tolterodine and alpha-blockers and/or 5-alpha-reductase inhibitors vs. tolterodine One RCT evaluated the efficacy of tolterodine extended release treatment for 1 year in older men with BPH treated with alpha-blockers and/or 5-alpha-reductase inhibitors. Treatment benefit was demonstrated in both groups with the only inter-group difference observed on the storage domain of IPSS score.[100] *Imidafenacin and tamsulosin vs. tamsulosin* One study was identified which assessed the effects of add-on treatment with imidafenacin on persistent overactive bladder symptoms in people receiving treatment with tamsulosin.[101] Improvements in frequencies of daytime urination, nighttime urination, urinary urgency, urgency incontinence, IPSS, HUS, IPSS-QOL, and BII, were significantly greater from 4 weeks through 12 weeks in the combination group. *Antimuscarinics plus alpha-blockers* Three systematic reviews and an RCT concluded that the evidence supports the efficacy and safety of antimuscarinics in combination with alpha-blockers in treating men with LUTS.[102-105] *Solifenacin and tamsulosin vs. placebo or tamsulosin* Five RCTs of solifenacin and tamsulosin combination therapy indicated improvements in some urinary outcomes compared with placebo or tamsulosin monotherapy.[106-110]		

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	Fesoterodine and tamsulosin vs. tamsulosin One RCT which assessed the efficacy and safety of fesoterodine extended-release plus tamsulosin in men with LUTS associated with BPH found a significant difference in storage and total IPSS values in the combination group.[111] Conversely, one RCT reported that tamsulosin and combination treatment both significantly improved LUTS symptoms but efficacy between two groups was not significant.[112] *Tolterodine and tamsulosin vs. tolterodine or tamsulosin* One study was identified which estimated the costs and QALYs associated with tolterodine extended release and tamsulosin for LUTS from the perspective of the UK healthcare system.[113] Tolterodine plus tamsulosin combination therapy appeared to be cost-effective compared with tolterodine or tamsulosin monotherapy or placebo in male patients with LUTS. The guideline recommends that men should be offered an anticholinergic as well as an alpha blocker if they still have storage symptoms after treatment with an alpha blocker alone. From an assessment of abstracts it was not specified whether men had previously received alpha blocker treatment. However, the results of the studies 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.		

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	Combination therapy (PDE5 inhibitor plus 5-alpha reductase inhibitor) *Tadalafi and finasteride* One RCT was identified which investigated the effects of tadalafil co-administered with finasteride over 26 weeks on LUTS.[114] The results indicated that co-administration of tadalafil / finasteride provided early LUTS improvement in men with BPH and prostatic enlargement. The guideline does not include recommendations on the use of PDE5 inhibitors and 5-alpha reductase inhibitor combination therapy for LUTS but currently there is insufficient new evidence to enable a recommendation to be made. ***Combination therapy (alpha blockers plus NSAID)*** *Celecoxib and terazosin vs. terazosin* One RCT which compared celecoxib plus terazosin with terazosin only in men with BPH found that the overall severity of symptoms, irritative symptoms, and prostate volume decreased more in the combined treatment group than in the control group.[115] The guideline does not include recommendations on the use of alpha blocker and NSAID combination therapy for BPH but currently there is insufficient new evidence to enable a recommendation to be made.		
In men with LUTS who are not on treatment, what are the most clinically effective and cost effective recall intervals for review for detecting progression of symptoms?			
No new key evidence was found for	No studies identified.	None identified.	No relevant evidence

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
this section.			identified.
In men with LUTS who take alpha blockers/5-alpha reductase inhibitors/anticholinergics/phosphodiesterase 5 inhibitors or combination therapy, what are the most clinically effective and cost effective recall intervals for review for detecting progression of symptoms?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
What is the effectiveness of holmium:YAG Laser Enucleation of Prostate (HoLEP) for treatment of LUTS?			
An RCT by Eltabey et al. (2010) assessed the safety, efficacy and medium-term durability of HoLEP combined with mechanical morcellation against the standard TURP in patients with bladder outlet obstruction due to BPH. The HoLEP group had a greater improvement in post-voiding residual urine volumes scores at 1-, 6- and 12 months versus the TURP group. In addition, Fayad et al. (2011) conducted an RCT comparing HoLEP with bipolar TURP in patients with BPH. HoLEP and bipolar TURP were equally effective in treating patients. The Evidence Update concluded that these studies add to the evidence base that was available during the development of CG97, which recommends either of these treatments.	*HoLEP vs. photoselective vaporisation of the prostate* An RCT was identified which compared HoLEP and photoselective vaporisation of the prostate as surgical treatment of prostatic adenomas greater than 60 ml[116] A significantly higher maximum flow rate and lower post-void residual urine were noted in holmium laser cases during follow-up. However, no significant difference in IPSS or QoL was detected between groups which is consistent with the evidence presented in the guideline. *HoLEP vs.TURP* Three RCTs comparing HoLEP with TURP found that both surgical treatments were equivalent in improving lower urinary tract symptoms.[117-119] This evidence is consistent with the evidence presented in the guideline. *HoLEP vs. plasmakinetic enucleation and resection of the prostate* Compared with plasmakinetic enucleation and resection of the prostate in men with bladder outflow obstruction from BPH, laser enucleation of the prostate had significantly shorter operative time, postoperative irrigation, time and catheterisation time.[120]	The GDG indicated that holmium laser therapy remains inaccessible in many areas.	New evidence is unlikely to impact on guideline recommendations.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	Ho:EP vs. thulium laser transurethral enucleation of the prostate One RCT compared thulium laser transurethral enucleation of the prostate with HoLEP in men with BPH.[121] At 18 months, the lower urinary tract symptom indexes were improved significantly in both groups compared with the baseline values. The quality of life score and peak urinary flow rate were similar between the 2 groups although thulium laser transurethral enucleation of the prostate was superior to HoLEP in blood loss and inferior to HoLEP in operation time. *Transurethral enucleation of the prostate vs. bipolar resection of the prostate* One RCT was identified which compared the clinical outcomes between thulium laser transurethral enucleation of the prostate and plasmakinetic bipolar resection of the prostate for treating BPH.[122] The results indicated that both interventions relieved LUTS equally, with high efficacy and safety. In summary, the guideline recommends that if surgery is offered for managing voiding LUTS then HoLEP should be one of the methods offered and no new evidence was identified which would invalidate this recommendation.		
What is the effectiveness of laser coagulation techniques for treatment of LUTS?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
What is the effectiveness of laser vaporisation techniques for treatment of LUTS?			

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
An RCT by Capitan et al. (2011) assessed the safety and efficacy of GreenLight HPS 120-W laser vaporisation compared with transurethral resection of the prostate (TURP) in men with LUTS caused by BPH. The Evidence Update concluded that long-term data would be needed to demonstrate lasting efficacy compared with the gold standard of TURP. As such, it was felt that this study has no impact on the guideline. A cost-effectiveness study by Armstrong et al. (2009) aimed to determine which of the surgical treatments available for LUTS associated with BPH is most cost-effective. The study 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. The Evidence Update concluded that this study is unlikely to affect CG97 as the results need confirmation in a good quality, prospective RCT.	One RCT was identified which found that photoselective vaporisation of the prostate was equally effective and safe as holmium laser ablation of the prostate in men with BPH.[123] In addition, the results of an RCT 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.[124] This new evidence is consistent with the evidence presented in the guideline. 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. Additional consistent conclusive new evidence is required before considering updating this review question.	The GDG suggested that the evidence base supporting the use of photoselective vapourisation of the prostate may be stronger than it was when the guideline was developed.	New evidence is unlikely to impact on guideline recommendations.
What is the effectiveness of transurethral microwave thermotherapy for treatment of LUTS?			
No new key evidence was found for this section.	A Cochrane systematic review was identified which assessed the therapeutic efficacy and safety of microwave thermotherapy techniques for treating men	None identified.	New evidence is unlikely to impact on guideline recommendations.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	with symptomatic benign prostatic obstruction.[125] The pooled mean urinary symptom scores decreased by 65% with TUMT and by 77% with TURP. The weighted mean difference for the IPSS favoured TURP although microwave thermotherapy improved IPSS symptom scores and peak urinary flow compared with sham procedures. The results of this study are in line with the evidence included in the guideline. 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 direction of this recommendation.		
What is the effectiveness of transurethral vaporisation of prostate for treatment of LUTS?			
No new key evidence was found for this section.	One RCT was identified which evaluated the safety and effectiveness of transurethral vaporisation of the prostate (TUVP) compared to the standard transurethral resection of the prostate (TURP) in the treatment of BPH.[126] The evaluation of IPSS scores, PVRU, Qmax, and prostatic volumes of the patients 1 month, 3 months, and 1 year postoperatively did not report any significant differences between the two groups. The results of this study are in line with the evidence included in the guideline and, since TUVP is recommended for use, are unlikely to impact on the guideline recommendations.	None identified.	New evidence is unlikely to impact on guideline recommendations.
What is the effectiveness of transurethral needle ablation of prostate for treatment of LUTS?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
What is the effectiveness of transurethral incision of the prostate for treatment of LUTS?			

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
What is the effectiveness of botulinum toxin for treatment of LUTS?			
No new key evidence was found for this section.	*Idiopathic detrusor overactivity* Two systematic reviews[127,128] and two RCTs[129,130] indicated that botulinum toxin has a positive effect on idiopathic 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* Three systematic reviews[131-133] and 3 RCTs[134-136] indicated a potential beneficial effect of botulinum toxin compared with placebo on overactive bladder symptoms. In addition, one RCT assessed the effects of botulinum toxin in patients with idiopathic overactive bladder and urinary urgency incontinence with or without detrusor overactivity, inadequately managed with anticholinergics.[137] Improvements in urodynamic parameters and clinical outcomes generally trended together following botulinum toxin treatment. Through an assessment of abstracts, however, it was not clear if the patient population in the studies included men. Since the guideline was published several RCTs and systematic reviews have reported a beneficial effect of botulinum toxin A for overactive bladder symptoms. The guideline algorithm indicates that injection of botulium into the bladder wall may be considered in men with symptoms of overactive bladder after	The GDG highlighted that new evidence has emerged on the use of botulinum toxin for LUTS whilst it is now licensed for the the management of bladder dysfunctions in adult patients who are not adequately managed with anticholinergics, such as overactive bladder. .	New evidence is unlikely to impact on guideline recommendations.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	conservative management and anticholinergics have failed and the identified new evidence supports this approach. *BPH* Two RCTs investigated the efficacy of different doses (100 U vs. 200 U and 100 U vs. 300 U) of botulinum toxin to treat LUTS associated with BPH with the doses demonstrating comparable efficacy.[138,139] One RCT compared botulinum toxin 100 U, 200 U, and 300 U with placebo and found no significant difference between botulinum toxin and placebo.[140] However, a post-hoc analysis 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 as the GDG expressed a desire to see stronger evidence on the efficacy and safety of botulinum toxin in the treatment of male LUTS and currently there is insufficient consistent new evidence to impact this recommendation.		
What is the effectiveness of transurethral vaporesection of the prostate for treatment of LUTS?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
What is the effectiveness of stents for treatment of LUTS?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
What is the effectiveness of high intensity focused ultrasound for treatment of LUTS?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
What is the effectiveness of transurethral ethanol ablation of the prostate for treatment of LUTS?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
What is the effectiveness of open prostatectomy for treatment of LUTS?			
No new key evidence was found for this section.	*Transvesical open prostatectomy vs. plasma enucleation of the prostate* Two RCTs comparing plasmakinetic enucleation of the prostate and transvesical open prostatectomy for BPH reported that both groups had a similar and significant postoperative improvement in IPSS, QOL, maximum uroflow rate (Qmax), postvoid residual (PVR) urine volume and prostate specific antigen.[141,142] *Transvesical prostatectomy vs. transurethral enucleation and resection of the prostate* One RCT comparing the efficacy and safety of transurethral enucleation and resection of the prostate and transvesical prostatectomy for BPH found that both interventions had similar efficacy.[143] *Bipolar transurethral plasmakinetic prostatectomy vs. thulium laser resection of the prostate* One RCT which compared the safety and efficacy of thulium laser resection of the prostate and bipolar transurethral plasmakinetic prostatectomy in men with BPH found similar and significant postoperative improvement in both groups for IPSS, QoL, Qmax and PVR at 3 months after the operation.[144] *Open prostatectomy vs. bipolar transurethral resection of the prostate* One RCT assessed the efficacy and safety of bipolar	None identified.	New evidence is unlikely to impact on guideline recommendations.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	TURP versus standard open prostatectomy in patients with LUTS due to bladder outlet obstruction.[145] Comparative data on IPSS symptom score, IIEF-5 and Qol, PSA, peak urinary flow rates and post-void residual urine volume in the 2 groups were similar although postoperative catheterisation, hospital stay and 3-yr overall surgical re-treatment-free rate were significantly better in the bipolar TURP group. 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. From an assessment of the abstracts, however, not all studies reported the size of prostates among included participants and any that did reported the prostate volume rather than the size in grams. However, the identified new evidence indicates that open prostatectomy has efficacy in men with BPH and is therefore unlikely to impact on the guideline recommendation.		
What is the effectiveness of transurethral resection of prostate for treatment of LUTS?			
An RCT by Fagerstrom et al. (2011) in men with BPH that did not respond to medical therapy, compared bipolar with monopolar TURP. Fewer readmissions were seen in the bipolar TURP group compared with the monopolar TURP group. However, there were no differences in hospital stay. In addition, a systematic review and meta-analysis by Mamoulakis et	*TURP vs. laser photoselection vaporisation* One RCT comparing photoselective vaporisation with TURP in men with LUTS due to BPH found that IPPS reduction at 2 yr, gain in Qmax and QoL were equivalent for both treatment modalities[146] whilst another RCT found that improvements in IPSS, QOL, prostate volume and Qmax at 12 months were similar in both groups.[147] In addition, noninferiority of photoselective vaporisation of the prostate compared with TURP was reported in an RCT.[148] Conversley,	The GDG mentioned that there are ongoing trials investigating TURP versus laser surgery.	New evidence is unlikely to impact on guideline recommendations.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
al. (2009) compared the effects of bipolar and monopolar TURP. No clinically significant differences were seen between the two treatment modalities with respect to short-term (12 months) efficacy. The Evidence Update concluded that the results of these studies showed no significant difference in short-term efficacy between the two treatment modalities, a finding consistent with the guideline, which recommends both approaches.	during the 1, 3, 6, 12, and 18 months' follow-up, the plasma vaporisation of the prostate group had significantly superior parameters in terms of IPSS and Qmax compared with TURP.[149] Two meta-analyses which assessed whether photoselective vaporisation has advantages over TURP in terms of effectiveness and safety for treatment of patients with BPH found no significant difference in IPSS and maximum flow rate at 6 month[150 151], 12 month[150], and 24-month follow-up[150]. Two additional systematic reviews also found that photoselective vaporisation of prostate and TURP had similar efficacy and safety.[152,153] One RCT assessed the efficacy and safety of bipolar plasma vaporisation of the prostate with "button-type" electrode against standard TURP for BPH.[154] Plasma vaporisation was significantly superior to TURP in terms of indwelling catheter time, blood loss, hospital stay, IPSS, QOL, Qmax, haemoglobin and operation time. One study was identified which compared photoselective vaporisation of the prostate with TURP in terms of their cost to the Greek National Health Service (NHS) or to the Public Insurance Sickness Funds (PISF).[155] The results indicated that photoselective vaporisation for 40 to 70 cc prostates was preferable from the perspective of the NHS. From the perspective of PISF, photoselective vaporisation was less costly only in the case of patients who are		

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	still working. *Monopolar vs. bipolar TURP* Eight RCTs[156-163] and a systematic review[164] found that monopolar and bipolar TURP both improved LUTS symptoms with no significant differences between the interventions. One of the RCTs reported that efficacy was comparable between arms at 5 years postyoperatively.[163] *TURP vs. thulium laser vaporesection of the prostate* One RCT comparing thulium laser vaporesection of the prostate with TURP in men with BPH found that acute complications, and improvements in IPSS and maximum urinary flow rates, were similar in both groups.[165] One study compared the efficacy and safety profile of bipolar hybrid prostate surgery using both resection and vaporisation modes, with bipolar resection undertaken using the transurethral resection in saline bipolar system in men with BPH.[166] The hybrid group had a significantly shorter postoperative catheter time. *TURP vs. HoLEP* A systematic review[167] and RCT[168] comparing TURP with HoLEP for BPH found that both interventions improved IPSS and Qmax. The review reported that the Qmax and IPSS in the HoLEP group were significantly better than those in the TURP group at 12 months postoperatively whilst the RCT found that patients in the HoLEP group displayed shorter		

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	catheter times and shorter hospital stays. Conversley, a meta-analysis comparing the efficacy and safety of TURP with HoLEP found the highest reduction of the IPSS in the TURP group.[169] *TURP vs. channel transurethral resection of the prostate (C-TURP)* The clinical effectiveness of channel transurethral resection of the prostate (C-TURP) combined with an interstitial laser coagulation (ILC) technique in men with BPH was assessed in an RCT.[170] The TURP group had the highest and the ILC group had the lowest increase in the Q max at the 12-, 24-, and 48-month follow-ups. *TURP vs. PlasmaKineticTM enucleation* One RCT compared the perioperative and postoperative characteristics of prostate PlasmaKineticTM enucleation and bipolar transurethral resection for large volume BPH.[171] 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. *TURP vs. transurethral incision of the bladder neck* The 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 was evaluated in an RCT.[172] At 6 months postoperatively, no significant		

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	difference in IPSS was observed between the two groups although the Qmax in patients receiving STRUP+TUIBN was markedly higher than in those receiving TURP. *General* One systematic review examined TURP as a treatment for LUTS due to BPH indicating that monopolar TURP reduced major morbidity.[173] The identified new evidence indicated that TURP has similar efficacy compared with laser photoselection vaporisation, thulium laser vaporesection of the prostate, HoLEP, plasmaKineticTM enucleation and transurethral incision of the bladder neck whilst there was no difference between monopolar or bipolar TURP. 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 and no evidence was identified which would change the direction of this recommendation.		
What is the effectiveness of bipolar resection of the prostate for treatment of LUTS?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
What is the effectiveness and comparative effectiveness of surgery in reducing storage symptoms?			
No new key evidence was found for this section.	One systematic review assessed the potential additional benefit of non-standard vs standard surgical treatments for BPH concluding that there was a lack of high-quality RCTs and trials designed to investigate non-inferiority.[174] A second systematic review	The GDG indicated that a large ongoing trial is comparing artificial urinary sphincter with male slings in men with post prostatectomy	New evidence is unlikely to impact on guideline recommendations.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	evaluated the use of the artificial urinary sphincter (AUS) for the surgical management of non-neurogenic stress urinary incontinence (SUI) in men.[175] Continence, evaluated only by patient-reported pad use and various questionnaires, was achieved in 61-100% of cases (no pad or one pad per day). 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.	incontinence.	
What is the effectiveness of medications compared to conservative therapies in managing LUTS?			
No new key evidence was found for this section.	One RCT and two systematic reviews compared antimuscarinics with conservative treatments including behavioural treatment (pelvic floor muscle exercises, urge suppression techniques, delayed voiding)[176]; bladder training[177] and percutaneous tibial nerve stimulation[178]. No significant difference was observed between groups in the RCT comparing drug therapy with behavioural therapy. In addition, the systematic review of percutaneous tibial nerve stimulation found limited evidence that this intervention may have similar efficacy to tolterodine. In contrast, the results of a Cochrane systematic review indicated that symptomatic improvement was more common amongst those participants on anticholinergic drugs compared with bladder training. The guideline recommends that men with LUTS should only be offered drug treatment when conservative therapy has failed or is not appropriate and currently there is	None identified.	New evidence is unlikely to impact on guideline recommendations.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	insufficient conclusive new evidence to change the direction of this recommendation.		
What is the effectiveness of conservative compared to surgical therapies in managing lower urinary tract symptoms?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
What is the effectiveness of medications compared to surgical therapies in managing LUTS?			
No new key evidence was found for this section.	One RCT was identified which compared the effect of tamsulosin versus transurethral resection of the prostate (TURP) for the management of nocturia in previously untreated men with LUTS suggestive of BPH.[179] Both interventions improved study outcomes although TURP was associated with a statistically significant improvement in the number of nocturnal awakenings and in the IPSS, ICIQ-N and ICIQ-NQol scores in comparison with tamsulosin. The guideline recognised the benefits of surgery but also considered the risk of harms however, adverse events associated with tamsulosin or TURP were not described in the included abstract. Due to the high costs of surgery the guideline recommends that surgical options should only be offered if other treatments have failed and currently there is insufficient new evidence to change the direction of this recommendation.	None identified.	New evidence is unlikely to impact on guideline recommendations.
What is the effectiveness of alpha blockers in treating men after acute urinary retention?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
What is the effectiveness of complementary and alternative therapies in managing LUTS?			
A systematic review by Tacklind et al. (2009) assessed the effects of the plant extract *Serenoa repens* in the	*Phytotherapy* Seven studies were identified evaluating Serenoa repens for management of LUTS. One study found a	None identified.	New evidence is unlikely to impact on guideline recommendations.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
treatment of LUTS associated with BPH. *Serenoa repens* was not more effective than placebo in improving IPSS urinary symptoms. The Evidence Update concluded that the results of this systematic review have no impact on the guideline which states 'do not offer' phytotherapy.	significant reduction in IPSS compared with placebo[180] although 6 of the studies reported no benefit of Serenoa repens over control.[181-186] One systematic review found that Cernilton was not more effective than placebo or comparative study agents in improving urinary flow rates, residual volume or prostate size in men with BPH.[187] Conversely, an overview of systematic reviews observed a significant improvement in BPH symptoms following treatment with Cernilton.[184] Overall, the identified new evidence is unlikely to change the direction of the current guideline recommendation which indicates that phytotherapy for LUTS in men should not be offered. *Supplements* The results of one RCT indicated a significant improvement in IPSS score, urodynamic parameters: maximal rate of urine flow (Qmax), average flow (Qave), V and RV, total PSA value and serum selenium levels in men with LUTS treated with a combination of selenium and silymarin.[188] One RCT found no difference in LUTS in men taking a daily 240 ml 100% grape juice versus placebo after 3 months.[189] One RCT was identified which assessed the efficacy and safety of soy isoflavones in controlling the symptoms and signs of LUTS due to BPH found a		

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	slight superiority of isoflavones over placebo over 12 months.[190] 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. *Posterior tibial nerve stimulation* The early clinical and urodynamic results of posterior tibial nerve stimulation in patients with refractory monosymptomatic nocturnal enuresis were evaluated in a placebo-controlled RCT.[191] All urodynamic parameters significantly improved in the posterior tibial nerve stimulation however, the response was not maintained in all participants at follow-up. This intervention is not currently considered in the guideline but it would be pertinent to wait for additional research on efficacy, benefits and harms before considering for inclusion in the guideline. *Tai chi* Tai chi was found induce a significant improvement in LUTS and QoL compared with a control group receiving usual care in one RCT.[192] However, as this was a small study with short-term follow-up (3 months), it would be pertinent to wait for further research on this intervention in LUTS before considering the impact on the guideline recommendations.		

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	Osteopathic treatment One RCT found a significantly greater improvement in IPSS following osteopathic treatment compared to control.[193] However, as this was a small study with short-term follow-up (3 months), it would be pertinent to wait for further research on this intervention in LUTS before considering the impact on the guideline recommendations.		
In men who report LUTS, what is the effect of acupuncture vs. no acupuncture or other conservative therapy on patient related and biometric outcomes and adverse events?			
No new key evidence was found for this section.	In summary, two studies on acupuncture for treatment of BPH or nocturnal enuresis were identified. One study evaluated the efficacy of acupoint electroacupuncture[194] whilst the second study[195] 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. As such, 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.	None identified.	New evidence is unlikely to impact on guideline recommendations.
What is the effectiveness and comparative effectiveness of homeopathy in reducing symptoms for managing LUTS?			
No new key evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
Does provision of information about management of LUTS improve patient outcomes?			
A post-hoc analysis by Yap et al. (2009) presented data from an RCT to assess the effect on voiding behaviour	One RCT indicated that self-management of LUTS improved IPSS scores and QoL at 6 months follow-up compared with standard care.[196] In addition, an	None identified.	New evidence is unlikely to impact on guideline recommendations.

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
of a self-management programme plus standard care versus standard care alone. The mean volume per void in the self-management group was 57 ml higher than in the control group at the 3-month assessment. It was concluded that this evidence would have no impact on the guideline.	economic evaluation reported that nurse specialist involvement for LUTS was recommended as a suitable intervention for primary care.[197] This evidence supports the evidence currently included in the guideline.		
Areas not currently included in the guideline			
In men who report LUTS, what is the effect of physical activity versus any other conservative therapy or no treatment on patient related and biometric outcomes and adverse events?			
No new key evidence was found for this section.	One RCT evaluated whether a training program designed to improve physical capacity among residents in nursing homes has any impact on urinary incontinence.[198] The intervention group had significant better results compared with the control group however, additional evidence on the benefits and harms in men with LUTS compared with other conservative therapies is needed before considering for inclusion in the guideline.	None identified.	Insufficient consistent conclusive evidence to consider for inclusion in the guideline.
What is the clinical and cost-effectiveness of mirabegron, duloxetine and isosorbide dinitrate for treatment of LUTS?			
No new key evidence was found for this section.	*Mirabegron* <u>Mirabegron vs. placebo</u> Five RCTs[199-203], a systematic review[204] and pooled data from three RCTs[205] indicated that mirabegron improved LUTS compared with placebo. <u>Mirabegron vs. tolterodine</u> The 12 month safety and efficacy of mirabegron compared with tolterodine for overactive bladder was evaluated in an RCT whereby both treatments	None identified.	In terms of mirabegron, the identified evidence indicates that this treatment has efficacy for LUTS. This drug therapy has been covered in the related Technology Appraisal TA290: Overactive bladder – mirabegron (published June 2013) which

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	improved key overactive bladder symptoms from the first measured time point of 4 wk, and efficacy was maintained throughout the 12-mo treatment period.[206] *Duloxetine* One RCT compared duloxetine with placebo in men with stress urinary incontinence after radical prostatectomy.[207] Reduction in incontinence episodes frequency was significant with duloxetine compared to placebo whilst duloxetine improved quality of life. *Isosorbide dinitrate* One RCT compared sublingual isosorbide dinitrate with placebo in men with BPH induced acute urinary retention indicating that the mean voided urine volume was greater in the intervention group compared with control.[208] In summary, there is insufficient evidence available to consider duloxetine and isosorbide dinitrate for inclusion in the guideline. In terms of mirabegron, the identified evidence indicates that this treatment has efficacy for LUTS. However, this drug therapy has been covered in a related Technology Appraisal: TA290 Overactive bladder – mirabegron (published June 2013).		recommends mirabegron as an option for treating the symptoms of overactive bladder only for people in whom antimuscarinic drugs are contraindicated or clinically ineffective, or have unacceptable side effects. This Technology Appraisal links to the drug treatment section of the lower urinary tract symptoms in men NICE pathway.
What is the effectiveness of prostatic urethral lift for treatment of LUTS?			
No new key evidence was found for this section.	Two RCTs comparing prostatic urethral lift with sham reported improvement in symptoms from baseline up to 12 months.[21,22] This intervention has been covered in a related Interventional Procedure IPG475: Insertion	Feedback from the GDG indicated that an RCT on the prostatic urethral lift procedure has published.	Prostatic urethral lift is an intervention not currently covered by the guideline. This is potentially a new

Conclusions from Evidence Update (March 2012)	Evidence/intelligence identified during the 4-year surveillance review (2014)	Clinical feedback from the GDG	Conclusion of the 4-year surveillance review (2014)
	of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia (published January 2014). The Interventional Procedure guidance recommended 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 provided that normal arrangements are in place for clinical governance, consent and audit.		intervention that could be considered alongside the other management options for BPH secondary to LUTS.

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