

Update summarising the conclusions of the international consultation on male lower urinary tract symptoms

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Abstract

The International Consultation on Urological Disease have recently published comprehensive conclusions, based on evidence reviewed by eight committees, on aspects of male lower urinary tract symptoms (LUTS). In this review, we summarise the conclusions from four

of the committees, namely, the evidence regarding the epidemiology of male LUTS, patient assessment, nocturia and medical management. It is indisputable that with an expanding and ageing global population the prevalence of male LUTS is likely to increase. Therefore symptom prevention and preservation of quality of life (QoL) feature highly in the guidelines. There are now a number of different medical options, proven to lead to significant improvements in symptom scores, flow rate and QoL available to men with LUTS. Meta-analyses have shown the benefits for alpha blockers, antimuscarinics, 5- α reductase and phosphodiesterase-5 inhibitors. High level evidence also exists for combinations of all of the above with alpha blockers and so men with concomitant storage symptoms, prostate volume > 30 mL, PSA > 1.4 or erectile dysfunction may be considered for combination treatment of an alpha blocker with an antimuscarinic, 5- α reductase inhibitor or phosphodiesterase-5 inhibitor respectively. In an era of personalised medicine, appropriate patient selection is likely to provide the key to the most effective clinical management strategy.

Key words: International consultation; Antimuscarinic; Male lower urinary tract symptoms; Guidelines; Nocturia; Epidemiology; 5- α reductase; Phosphodiesterase-5 inhibitors; Alpha antagonist

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Core tip: Men with lower urinary tract symptoms (LUTS) should be assessed not only for symptom severity and bother but also for risk of progression. Men with a PSA > 1.4 or a prostate larger than 30 mL should be considered for therapy to reduce prostate volume. With the options for management of men with LUTS also involving antimuscarinics, B3 agonists, phosphodiesterase inhibitors and a plethora of surgical options, a personalised approach is required. This is intended will lead to greatest patient satisfaction and improvement in quality of life.

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INTRODUCTION

The International consultation on male lower urinary tract symptoms (LUTS) took place in Fukuoka, Japan between 30th September and 4th October 2012. This was under the auspices of the Societe Internationale d'Urologie. One of the authors of this review was the co-chair for the consultation, which consisted of more than 50 international experts in LUTS.

Committees reviewed the evidence for eight different aspects of male LUTS. These included; epidemiology and natural history, aetiology and patient assessment, nocturia, sexual dysfunction, surgical therapies, detrusor underactivity, chronic pelvic pain and medical treatments for male LUTS.

For each topic, specific questions were raised by the committee members, followed by analysis and grading of the literature using the recommendations from the Oxford centre for evidence based medicine. In this article we hope to summarise the conclusions of four of the committees in the consultation regarding male LUTS. More information regarding the full guidelines can be found at the following address: <http://www.icud.info/publications.html>.

EPIDEMIOLOGY AND NATURAL HISTORY

The majority of epidemiological studies assessing LUTS have reported prevalence of symptoms in a population which tend to vary due to the methodology of data acquisition. Prevalence estimates for an elevated International Prostate Symptom Score (IPSS) score above eight range from 16% to 52%^[1-4]. A pooled analysis of 126 studies has shown an increase in urinary incontinence prevalence with age from 21% to 32% for elderly men^[5]. The prevalence of daily urinary incontinence in this analysis was reported at 9%.

More recent studies have assessed the individual symptoms captured in the IPSS with a more complete analysis of storage, voiding and post micturition symptoms as defined by the International Continence Society (ICS)^[6,7]. Nocturia and terminal dribbling are the most commonly reported storage and voiding symptoms. However, LUTS more often occur in clusters than in isolation, with overactive bladder (OAB) accounting for a prevalence of 10% to 25% as a cluster of urgency, frequency with or without nocturia^[8].

The longest follow up study of the prevalence of symptoms has shown a significant increase in LUTS over an 11 year period with a mean annual incidence of 3.7% for OAB and 0.8% for incontinence^[9]. In a

systematic review, 21 population based cohort studies were identified which looked at the natural history of LUTS^[10]. Of these only five included men with LUTS with no studies looking at symptoms in men younger than 40 years. Urinary flow rates have also been shown to decrease from age 50^[11].

Moreover, the importance of these symptoms in relation to effects on quality of life QoL and treatment seeking has been reported to be 50% and 20% respectively^[12]. This suggests that not all symptoms require treatment from the individual's perspective and prevalence data may over-estimate true symptomatic burden.

The most well reported risk factor found to be associated with the development of LUTS is age^[13]. Although LUTS are often considered a part of ageing, certain modifications to the behaviour of older men have been shown to alter this risk. Physical activity has been found to be protective reducing risk by 29%, whereas a BMI > 30 raises the risk of LUTS by 41%^[14]. Associations between metabolic syndrome and LUTS have shown mixed correlations with some studies reporting no association^[15,16]. Foodstuffs associated with LUTS include, dietary sodium, high doses vitamin C and a high alcohol intake^[17,18]. A recent meta-analysis has assessed genetic polymorphisms associated with male LUTS^[19]. The rs731236 variant of the vitamin D receptor was found to have a consistent protective effect against LUTS in different populations. The genomic approach is only beginning to reveal the potential inherited risks in developing LUTS. Conclusions from this section are shown in Table 1.

AETIOLOGY AND PATIENT ASSESSMENT

In order to describe the aetiology of LUTS, the committee firstly define what normal LUTS function should include. The Dutch population based Krimpen study provides good estimates of frequency and voided volumes. A frequency of greater than eight in 24 h is considered high and an average void of 246 mL is reported for men 50-78 years^[20]. It is suggested that a cut off of eight voids/d is not utilised as this may vary depending on age, social and climacteric factors. The maximal voided volume (formerly known as functional bladder capacity) was found to be 400 mL.

Frequency with a reduced voided volume has a number of explanations, which include; detrusor overactivity (DO), significant post voiding residual volume, inflammatory bladder conditions, malignant bladder conditions, fear of incontinence or retention and sensory bladder dysfunction. If the bladder capacity is also found to be reduced under general anaesthesia then this may be due to fibrosis or inflammation or may be seen post radiotherapy or following surgery leading to a reduced capacity bladder.

Urgency is the hallmark symptom of OAB symptom syndrome and the symptom therefore has the same prevalence as OAB. Strictly, there is no gradation of the

Table 1 Conclusions for epidemiology section

UI has a prevalence of 21%-32% in elderly men
OAB symptom cluster occurs in 10%-25% of men
Age is the strongest risk factor for LUTS

LUTS: Lower urinary tract symptoms; OAB: Overactive bladder; UI: Urinary incontinence.

symptom and it is defined, at least by the ICS, as an all or nothing sensation^[21]. The ability to defer micturition from the onset of urgency and the time between symptoms will clearly affect an individual's QoL. Factors influencing the occurrence of incontinence include urethral sphincter tone, mobility and toilet access.

In two-thirds of patients with OAB, DO may be observed on urodynamic assessment. The aetiology of DO has many proposed mechanisms. The two main mechanisms are neurogenic and myogenic. With neurogenic aetiologies, the cited evidence links to the appearance of DO with spinal and suprapinal pathologies secondary to activation of C-fiber afferents^[22]. With the myogenic theory, patchy denervation of muscle is proposed to lead to increased spontaneous contractions of detrusor muscle^[23]. Another potential aetiological contributor is detrusor ischaemia. Ischaemic bladders have been shown to have increased DO in a rabbit model of iliac artery injury^[24]. Other mechanisms include the degeneration of post synaptic nerves in the detrusor muscle and excess release of neurotransmitters and reactive oxygen species from ischaemic muscle.

Similar to all national and international guidelines, the consultation recommends a relevant history and clinical examination of the male with LUTS. The clinical examination should include a digital rectal examination of the prostate. Thereafter, a useful tool in assessing LUTS is the frequency- volume chart which has been shown to have greater accuracy over questionnaires^[25]. The optimal duration of the frequency-volume recordings is still under debate with longer periods offering more data but risk non-compliance^[26]. Generally, a 3 to 7 d chart is considered acceptable.

The use of the IPSS is also recommended as it has been tested psychometrically, is responsive to change and has been used extensively. It is however, not disease specific and therefore not a diagnostic tool and only 3 of the questions deal with the bothersome storage symptoms. It also correlates poorly with urodynamic assessment^[27]. It also does not assess urgency incontinence. Other questionnaires designed specifically for male LUTS include the ICIQ questionnaires and the Dan-PSS. These have been psychometrically tested. The ICIQ-MLUTS contains 22 questions and has been shown to be responsive to change^[28]. Similarly the DAN-PSS has good test-retest validity and also is unique as it derives a score by multiplying the bother caused by symptoms with severity^[29].

The use of urinalysis in the assessment of men with LUTS has received some thought recently due to the lack

of evidence of clinical benefit. However, it is recognised as a cheap and non-invasive test which could rule out potentially life threatening causes and so remains in the guidelines.

The medical therapy of prostatic symptoms study has shown that the risk of developing renal impairment from LUTS to be < 1% and therefore it was recommended that renal function should not be assessed as routine in men with LUTS^[30]. However, a recent Korean study has reported a reduction in GFR with severity of LUTS in older men and therefore it is kept in the guidelines^[31].

Serum PSA may be measured for two reasons, to screen for prostate cancer or to guide discussions regarding progression of LUTS. To date there is no consensus on the use of PSA to screen for prostate cancer but its use in detecting men at risk of progression is recognised^[32]. Therefore it is recommended for men according to national guidelines.

Post void residual urinary volume assessment and uroflowmetry are simple non-invasive office based assessments which are recommended based on expert opinion. Neither can distinguish between detrusor underactivity and bladder outflow obstruction. However, a significantly elevated post void residue may lead to harmful sequelae.

A myriad of imaging modalities have been reported to be useful in the assessment of the male with LUTS. Ultrasound assessment of prostate size, prostatic protrusion/angle and bladder weight/thickness are discussed. Their reproducibility, standardisation, sensitivity and specificity are inferior to formal urodynamic assessment and therefore these have not been recommended in the guidelines^[33].

Urodynamic assessment should always be performed according to good urodynamic practice guidelines. Due to its invasiveness its use should be restricted to men where a diagnosis is required or where the findings will change management. In addition, it may be useful to obtain information about other aspects of LUT function and dysfunction. It is also recommended to understand reasons behind treatment failure.

The committee discuss the usefulness of diagnosing DO. It is argued that 60% of OAB dry and 84% of OAB wet men have DO^[34]. Also 15% of healthy individuals will show this sign on urodynamic assessment^[35]. The finding, if associated with bladder outflow obstruction may resolve in 50%-70% of cases after a TURP^[36]. The reproducibility of this finding is also questioned^[37]. Therefore the use of urodynamic assessment should be undertaken by a clinician with sufficient understanding and clear questions in mind.

The more definitive use of urodynamics is in the assessment of obstruction and detrusor underactivity. The ICS nomogram is recommended for distinguishing these with the bladder outflow obstruction index being the important calculated parameter. During repeat testing only 1% of men changed category from obstructed to non- obstructed. The diagnosis of detrusor underactivity is reported to be under-recognised. In a study of 2066

Table 2 Conclusions for assessment section

History and examination are mandatory
Frequency volume chart is recommended for 3-7 d
The IPSS is recommended but it is not disease specific
Urine dipstick assessment is recommended to exclude serious underlying conditions
Serum creatinine estimation is still recommended
PSA should be performed according to national guidelines
Flow rate and post void residual estimation are recommended
Prostatic protrusion/angle and bladder weight/thickness are inferior to cystometry
Cystometry should be limited to men where a finding will change management

IPSS: International Prostate Symptom Score.

neurologically normal individuals 224 were shown to have this urodynamic finding^[38]. These men were shown not to benefit from bladder outflow obstruction surgery. Conclusions from this section are reported in Table 2.

NOCTURIA

Nocturia is likely to occur consequent upon a spectrum of clinical conditions. The agreed terminology states one should wake to void with the intention of returning to sleep. Clearly, an adjustment is required for those who work night shifts or those who sleep for short intervals. Nocturia not only impacts upon sleep and QoL but has also been shown to affect morbidity and mortality. In a Japanese study, nocturia twice at night doubled the risk of fractures and mortality^[39]. Its association with daytime fatigue, reduced work productivity and reduced vitality is also recognised^[40,41].

In the assessment of men with nocturia, it is imperative to differentiate those with nocturnal polyuria (> 20% and 33% of urine output during sleep relative to the day in young and older individuals respectively)^[21]. Another important parameter is the maximum voided volume (functional bladder capacity). If nocturnal urine production is greater than functional bladder capacity then an individual will be forced to wake from sleep to void. Another classification proposed by the committee is the division into pathological and non-pathological nocturia. The latter essentially involves waking for another reason such as external noises which lead to a convenience void. Conversely, the former occurs due to medical factors affecting sleep or urine storage.

Pathological nocturia may be divided into five categories: (1) reduced bladder capacity; this may be due to bladder fibrosis, previous surgery, radiation, OAB syndrome and bladder outflow obstruction; (2) global polyuria; this is often due to an undiagnosed endocrine abnormality such as diabetes mellitus, diabetes insipidus, polydipsia, hypercalcaemia or pharmacotherapy; (3) nocturnal polyuria which may be secondary to congestive cardiac failure, autonomic neuropathy, hypoalbuminaemia and nephrotic syndrome. Other causes include disruption to the secretion of vasopressin, drugs

and obstructive sleep apnoea; (4) sleep disorders including insomnia, sleep walking and drugs; and (5) mixed disorders resulting from a combination of the above.

When assessing a patient with nocturia it is also desirable to investigate risk factors. In the Finnish Nocturia and Overactive bladder study half of men with benign prostatic enlargement had nocturia^[42]. Men with major depression have a 2-6 fold increased risk of nocturia compared to those without^[42,43]. Obesity is also linked with a 2-3 fold risk of nocturia^[44]. One in three patients with nocturia in a Finnish study also reported urgency, however of those with OAB, 50% have nocturia^[45].

Very few national and international guideline committees have developed nocturia guidelines separately to other LUTS. The Japanese clinical guideline recommends differentiating nocturia into nocturia only, nocturia with diurnal frequency without other LUTS and nocturia with diurnal frequency with other LUTS. It is only the latter category which should be referred to urologists.

Management should follow a stepwise approach. Conservative measures should include fluid and caffeine restriction in the evening, leg elevation during the day and mid-afternoon diuretics and elasticated stockings. A systematic review has shown no discernible benefit of 5- α reductase inhibitors in improving nocturia although it is accepted some elderly men may see a reduction in nocturia frequency^[46]. Alpha antagonists on the other hand have been shown to decrease nocturia frequency over placebo^[47]. However, the majority of studies reporting this included men with benign prostatic obstruction symptoms. Combinations of the above two drug classes have also shown significant benefits for patients with nocturia. Similarly, the combination of an antimuscarinic agent and an alpha antagonist has shown clinically significant improvements over placebo^[48].

Antimuscarinic agents are only useful in reducing nocturia when it is associated with OAB^[49]. In non OAB patients the benefit is not so apparent. Desmopressin has been shown in a meta-analysis to safely reduce nocturnal frequency, delay time to first void and improve sleep quality^[50]. In a 12-mo extension study the reduction in nocturia episodes was still reduced significantly in 67% of men. The guidelines do however, recommend monitoring of sodium levels due to the risk of hyponatraemia. Another pharmacotherapeutic option includes the use of a diuretic 6 h prior to sleep. This has been shown to reduce nocturia by 0.5/night over placebo^[51].

Non Steroidal Anti-inflammatory Drugs may reduce nocturnal frequency but their use beyond 3 mo is not recommended due to the harms outweighing the benefits^[52]. Two phytotherapies have been shown in randomised trials to lead to a reduction in nocturia episodes, pygeum africanum and secale cereal^[53,54]. The former was shown to lead to a 19% reduction and the latter halved the nocturia frequency. The trials included in these trails are of a short duration, with limited numbers

Table 3 Conclusions for nocturia section

Nocturia frequency more than twice increases morbidity and mortality
It is important to differentiate nocturia from nocturnal polyuria, global polyuria and sleep disorders
Drugs shown to improve nocturia include alpha antagonists, and antimuscarinics, which may be combined
No overall benefit has been shown for 5- α reductase inhibitors but these may be useful for some men
Desmopressin has been shown to be beneficial but caution should be applied in renal failure and elderly patients
Diuretics are useful in specific cases
Benzodiazepines may be used to improve sleep quality

and so the data should be used with caution. Finally, benzodiazepines may be used to promote sleep. These are thought to affect nocturia only *via* an indirect effect by improving sleep^[55].

Procedures such as TURP to de-obstruct men with bladder outflow obstruction have been shown to reduce nocturia^[56]. These procedures should not be used in men without symptoms of obstruction and men should be counselled about adverse events prior to embarking upon surgery. Conclusions from this section are reported in Table 3.

MEDICAL TREATMENTS FOR MALE LUTS

Phytotherapies for the treatment of male LUTS were reviewed by this committee. The committee acknowledged the large number of publications with phytotherapies. Unfortunately the majority suffered from a lack of scientific rigor. However, some RCT's did exist. Of the phytotherapies, *Serenoa repens* (Saw palmetto) was the most investigated. A meta-analysis which looked at 14 RCT's showed Permixon (commercially available Saw palmetto) led to a reduction in IPSS of 4.8, increase in Qmax of 1.2 mL/s without changes in prostate volume or PSA^[57]. The most recent Cochrane review has shown no significant benefit to LUTS with *Serenoa repens* and therefore it is not recommended by the committee^[50].

Pygeum Africanum has been compared to placebo in 18 RCT's. It is shown to lead to improvements in symptoms and flow rate. However, the majority of RCT's were of a low quality and the results were not reported in a manner which permitted meta-analysis^[58]. Similarly, *Secale cereale* has been reported in two RCT's of poor quality and a meta-analysis was withdrawn from the literature in 2011^[59].

Four RCT's have assessed β -sitosterol. The trials were of moderate quality and showed a weighted mean difference in IPSS of 4.9 points and improvement in Qmax of 3.9 mL/s^[60]. Mild adverse events were reported. The long term effects of β -sitosterol remain unknown and therefore the committee have given no recommendation to this pending more data. Similarly, *Urtica dioica* has been shown to have superiority over placebo in RCT's of moderate quality. Improvements in IPSS, Qmax, and post void residual volume are reported. The agent

has also been compared to tamsulosin and finasteride and has been found to be non-inferior^[61,62]. No current recommendation is made pending further data.

The use of α 1a and α 1d selective blockers are recommended due to reduced systemic side effects. The α 1a components work on the prostate and bladder neck and the α 1d on the bladder and spinal cord. Twelve meta-analyses have shown the efficacy α of blockers^[63]. Data on efficacy and adverse events exists to beyond five years. A new selective α blocker -Silodosin- has shown significant improvement over placebo in IPSS, Qmax and also led to better improvement in voiding symptoms over tamsulosin but higher incidence of retrograde ejaculation^[64]. Urodynamically α antagonists lead to reduction in PdetQmax of 10-20 cm H₂O and increase Qmax by 2-3 mL/s^[65].

In this section, it is acknowledged that the majority of patients in trials of antimuscarinics are women. Kaplan *et al*^[66] were unable to demonstrate efficacy with tolterodine in men with storage symptoms. However, Herschorn *et al*^[67] have conducted a meta-analysis of fesoterodine 4 and 8 mg and found a reduction in frequency, urgency and voided volumes. The risk of retention was not apparently increased in these studies.

Combination therapy is considered a useful treatment option in men with both storage and voiding symptoms. Seven RCT's have shown the superiority of combination treatment over single agent treatment and placebo. It is argued that the symptomatic differences are small but significant. However, a trial powered to assess perception of treatment benefit showed a significant difference suggesting this difference is still important to patients^[68]. It should also be noted that these trials have selected men with a predominance of storage symptoms which should not be generalised to all men with LUTS. In addition, the majority of exclusion criteria for these trials include men with a post void residue < 250 mL and it must be recognised that men with larger residuals have not been investigated.

Androgens are implicated in the development of BPH and it has long been known that surgical castration may relieve urinary retention due to BPO. The use of luteinizing hormone releasing hormone (LHRH) agonists has been shown to reduce prostate volume by 25%, improve the IPSS score and Qmax but requires long term continuation^[69]. This is often met with the side effects of androgen deprivation such as reduced libido, impotency and hot flashes. On the other hand, LHRH antagonists (cetorelix and ozarelix) have failed to show superiority over placebo. Degarelix has not been studied in a placebo controlled RCT in men with LUTS/BOO. Thus the recommendation of the committee is that LHRH agonists may be used in carefully selected men who are not surgical candidates and LHRH antagonists are not recommended.

Multiple large RCT's have demonstrated the efficacy and safety of finasteride^[70,71]. The studies quote a 6%-10% risk of sexual dysfunction with placebo having up to 6% risk. Long term safety up to 10 years has also

Table 4 Conclusions for medical therapies section

Phytotherapies are not recommended due to evidence from meta-analysis or poor RCT data
Alpha antagonists are recommended
Antimuscarinic agents have mostly been trialled in women, but there is evidence to show their efficacy
Men in antimuscarinic trials have a post void residual of < 250 mL
Men with a PSA > 1.5 or prostate volume > 30 mL are more likely to benefit from a 5- α reductase inhibitor
Combination treatments may be suitable for some men
Discontinuation of the 5- α reductase inhibitor is not recommended as the symptoms are likely to return
Phosphodiesterase inhibitors may be used in men with a combination of LUTS and erectile dysfunction

LUTS: Lower urinary tract symptoms; RCTs: Randomized controlled trials.

been shown^[72]. With finasteride a reduction of 3 point on the IPSS score is seen from 6 mo through to 4 years. Also an improvement in Qmax of 2 mL/s is reported. However, it has been shown that not all men benefit from finasteride. Meta-analysis has revealed men with a PSA > 1.5 or prostate volume > 30 mL are more likely to obtain benefit^[73]. The mean change in prostate volume is 20% and a 50% reduction in PSA after 6 mo. Long term studies have shown a reduction in acute urinary retention rates from 2.7% to 1.1%. The proscar long term efficacy and safety study revealed a risk reduction of requiring TURP from 10% to 5%^[30]. Clearly, the reduction of risk for acute retention and need for surgery will depend on the characteristics of the selected population and those with a poorer flow rate, larger prostate and higher PSA are at increased risk of progression and thus more likely to benefit from this therapy^[74].

Dutasteride inhibits both isoenzymes of 5- α reductase and thus a more profound reduction in intraprostatic dihydrotestosterone levels is seen (95% vs 70%)^[75]. Similarly multiple RCT's have demonstrated efficacy in symptom improvement, flow rate and QoL up to two years and is summarised in a meta-analysis^[76]. An open label study, where the placebo group were switched to dutasteride and the dutasteride group continued follow up, showed lesser improvements in the group which was switched compared to the group already taking dutasteride suggesting earlier commencement of the drug leads to greater benefit than later initiation^[30]. All men selected for the dutasteride studies had a prostate volume > 30 mL and/or a PSA > 1.5 ng/mL. This may explain differences between the findings in these trials compared to those for finasteride.

The Enlarged Prostate International Comparator Study trial has compared 12-mo outcomes in men randomised to dutasteride or finasteride^[77]. The improvements in IPSS were 5.8 and 5.5 points and in Qmax 2 and 1.7 mL/s respectively. Another important study looked at the effect of discontinuation of finasteride and dutasteride^[78]. All participants took either finasteride or dutasteride with tamsulosin for one year and then stopped the 5- α

reductase inhibitor. After one year of discontinuation prostate volume and PSA levels returned to 90%-95% of baseline. Therefore discontinuation is not recommended. The PCPT and REDUCE trials reported a relative risk reduction of 40% of developing clinical BPH with the use of finasteride over 7 years or dutasteride over 4 years respectively^[79].

The committee also reviewed the use of phosphodiesterase-5 inhibitors in men with benign prostatic obstruction. Four RCT's have assessed tadalafil, one sildenafil and one vardenafil. Improvements are shown in IPSS, Qmax and IIEF scores. Only one study has compared tadalafil to tamsulosin and shown similar improvements in IPSS and flow rate between the drugs^[80]. One open label study has shown continued improvements up to one year^[81]. Adverse events are reported in a meta-analysis and include flushing, gastro-oesophageal reflux, headache, dyspepsia, back pain and sinusitis^[82].

The combination of alpha antagonists and 5- α reductase has been reviewed in a recent systematic review^[83]. Three studies have investigated combination treatments vs placebo. The largest studies are the MTOPS and CombAT^[84]. The former assessed the risk of progression in 3047 men with moderate to severe LUTS. The use of doxazosin alone reduced this risk by 39%, finasteride by 34% and combination therapy by 66%. However, the risk of requiring invasive treatment was only seen to be delayed by doxazosin compared to finasteride which reduced the risk. The latter study randomised 4500 patients to one of placebo, tamsulosin, dutasteride or combination. The major difference between this and the MTOPS study was the inclusion of only men with prostate volumes greater than 30 mL in the CombAT study. In this study, dutasteride was superior to tamsulosin but only after 18 mo. Combination was however superior to both individual therapies and placebo.

There are five non-placebo controlled randomised studies assessing the use of alpha blockers and phosphodiesterase-5 inhibitors as combination therapy compared in a meta-analysis^[82]. Improvements in IPSS and Qmax were significantly greater than alpha blockers alone. More importantly, the combination was reported to be safe with no reported serious adverse events. Patients individual circumstances should dictate if combination therapy and if so which combination therapy is required. Conclusions from this section are reported in Table 4.

CONCLUSION

We hope to have provided you with the highlights and evidence from the international consultation on male LUTS. It is always important to recognise the limitations of guidelines in that they provide us with up to date evidence which is stratified by quality but patients in the majority of RCT's have been included on the basis of strict criteria which will not always fit with real life patients. It is always important to treat the individual

patient but knowing the evidence behind our decision making will hopefully lead to better patient care.

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