INTERNATIONAL JOURNAL OF UROLOGY
International Journal of Urology (2021) doi: 10.1111/iju.14492

Guideline

Clinical Guidelines for Female Lower Urinary Tract Symptoms (second edition)

Satoru Takahashi,[1] Mineo Takei,[2] Hirotaka Asakura,[3] Momokazu Gotoh,[4] Osamu Ishizuka,[5] Kumiko Kato,[6] Masayasu Koyama,[7] Masami Takeyama,[8] Hikaru Tomoe,[9] Tomonori Yamanishi,[10] Osamu Yokoyama,[11] Masaki Yoshida,[12] Yasukuni Yoshimura[13] and Tsuyoshi Yoshizawa[1]

[1]Department of Urology, Nihon University School of Medicine, Tokyo, [2]Department of Urology, Harasanshin Hospital, Fukuoka, [3]Department of Urology, Saitama Medical University, Iruma, [4]Department of Urology, Nagoya University Graduate School of Medicine, Nagoya, [5]Department of Urology, Shinshu University School of Medicine, Matsumoto, [6]Department of Female Urology, Japanese Red Cross Nagoya First Hospital, Nagoya, [7]Department of Obstetrics and Gynecology, Osaka City University Graduate School of Medicine, Osaka, [8]Urogynecology Center, First Towakai Hospital, Takatsuki, [9]Department of Urology, Tokyo Women's Medical University Medical Center East, Tokyo, [10]Department of Urology, Continence Center, Dokkyo Medical University, Tochigi, [11]Department of Urology, Faculty of Medical Science, University of Fukui, Fukui, [12]Department of Urology, National Center for Geriatrics and Gerontology, Obu, and [13]Female Pelvic Health Center, Showa University Northern Yokohama Hospital, Yokohama, Japan

Abbreviations & Acronyms
CLSS = Core Lower Urinary Tract Symptom Score
CQ = clinical question
ES = electrical stimulation
FLUTS = female lower urinary tract symptoms
ICIQ-SF = International Consultation on Incontinence Questionnaire-Short Form
IIQ = Incontinence Impact Questionnaire
IPSS = International Prostate Symptom Score
I-QOL = Incontinence Quality of Life scale
KHQ = King's Health Questionnaire
LUTS = lower urinary tract symptoms
MUS = midurethral sling
N-QOL = Nocturia-Quality of Life questionnaire
OAB = overactive bladder
OAB-q = overactive bladder questionnaire
OABSS = Overactive Bladder Symptoms Score
P_{det} = detrusor pressure
PFMT = pelvic floor muscle training
Q_{max} = maximum urinary flow rate
RCT = randomized controlled trial
SNM = sacral neuromodulation
TOT = transobturator tape
TVT = tension-free vaginal tape

Correspondence: Satoru Takahashi M.D., Department of Urology, Nihon University School of Medicine, 30-1 Oyaguchikami-machi, Itabashi-ku, Tokyo 173-8610, Japan. Email: takahashi.satoru@nihon-u.ac.jp

Received 23 October 2020; accepted 13 December 2020.

Abstract: The present article is an abridged English translation of the Japanese Clinical Guidelines for Female Lower Urinary Tract Symptoms (second edition), published in September 2019. These guidelines consist of a total of 212 pages and are unique worldwide in that they cover female lower urinary tract symptoms other than urinary incontinence. They contain two algorithms for "primary treatment" and "specialized treatment," respectively. These guidelines, consisting of six chapters, address a total of 26 clinical questions including: (i) treatment algorithms; (ii) what are female lower urinary tract symptoms?; (iii) epidemiology and quality of life; (iv) pathology and illness; (v) diagnosis; and (vi) treatment. When the patient's symptoms mainly involve voiding and post-micturition symptoms, specialized treatment should be considered. In the event of voiding symptoms concurrent with storage symptoms, residual urine should be measured; if the residual urine volume is <100 mL, then diagnosis and treatment for storage symptoms is prioritized, and if the volume is ≥100 mL, then specialized treatment should be considered. When storage symptoms are the primary condition, then the patient is subject to the primary treatment algorithm. Specialized treatment for refractory overactive bladder includes botulinum toxin injection and sacral nerve stimulation. For stress urinary incontinence, surgical treatment is indicated, such as urethral slings. The two causes of voiding symptoms and post-micturition symptoms are lower urinary tract obstruction and detrusor underactivity (underactive bladder). Mechanical lower urinary tract obstruction, such as pelvic organ prolapse, is expected to improve with surgery.

Key words: female, guideline, lower urinary tract symptoms, overactive bladder, stress urinary incontinence.

Introduction

The first edition of the Japanese Clinical Guidelines for Female Lower Urinary Tract Symptoms[1] was published in November 2013. These were the world's first guidelines that comprehensively addressed the treatment of FLUTS. Six years after the first edition, a revised version of the guidelines is presented here.

The research subjects included adult women with LUTS complaints of some kind. The symptoms of girls (age <18 years) and elderly women requiring nursing care have a different pathology and are thus not included. These guidelines are intended to be used primarily by urologists and health professionals such as doctors, nurses, and public health nurses who are engaged in the medical care of patients with a broad range of LUTS, and contain two algorithms for "primary treatment" and "specialized treatment", respectively.

Methods

Committee members recommended by the Japanese Continence Society (authors of the present paper) created a draft by collecting and carefully reading articles. Thereafter, the draft manuscript was proofread by the evaluation committee and board of directors of the Japanese Continence Society and the Japanese Urological Society. Following this, public comments were obtained and the manuscript was corrected and completed. Furthermore, cooperation was obtained from the Japanese Society of Female Pelvic Floor Medicine.

Articles were collected using the PubMed and MEDLINE databases, and articles from September 2011 to 2018 were searched (including those in ePUB format). Articles in Japanese were searched using the JAMAS database (Ichushi-Web). Articles cited in the searched articles and other related articles (including those published prior to 2011 and after 2018) were used as needed. Furthermore, some articles cited in the first edition of the Japanese Clinical Guidelines for Female Lower Urinary Tract Symptoms,[1] as well as resources obtained by methods other than our search, such as Diagnostic Procedure Combination payment data and announcements by the U.S. Food and Drug Administration, were included. Moreover, in addition to existing guidelines[2,3] in Japan, we referred to the guidelines for urinary incontinence of the American Urological Association and European Association of Urology,[4,5] as well as the publication by the International Consultation on Incontinence, "*Incontinence*", Sixth edition, 2017[6].

The level of article (I to V) was determined for articles pertaining to treatment. The grade of recommendation was determined to reflect the discussion and agreement of committee members upon close examination of the consistency of the conclusion, effect size, applicability, and treatment characteristics, such as adverse reactions and cost, for the level of evidence drawn from the articles (consensual recommendation; Table 1).

The content recommended in these guidelines is based on scientific grounds and is not influenced by the interests of any particular group, product, or technique. The costs associated with creating these guidelines were met by a guideline creation grant from the Japanese Continence Society. Furthermore, conflicts of interest of each member and director were disclosed to the Japanese Continence Society, and the absence of any serious conflicts of interest was verified by the ethical review board.

Table 1 Grade of recommendation

Grade	Description
A	This action is strongly recommended
B	This action is recommended
C	There are no clear evidence for recommending this action
C1	Performing the action is not recommended
C2	Not performing this action is recommended
D	The action can still be performed
Pending	No decision has been made regarding the grade of recommendation

The grade of recommendation is determined after discussion and agreement by members regarding: (i) the level of evidence; (ii) variation in conclusions; (iii) size of the effect; (iv) clinical applicability; and (v) adverse drug reaction or cost.

Algorithm

Figures 1 and 2 present the "algorithm for primary treatment", and the "algorithm for specialized treatment," respectively.

Subjects of primary treatment include patients without any medical history or findings that would pose a problem and those who present with a chief complaint of storage symptoms.

Selected CQs

Among the 26 CQs, we present the main CQs and their summaries.

CQ6. What type of LUTS are associated with pelvic organ prolapse?

Summary: Pelvic organ prolapse is often accompanied by both storage and voiding disorders.[7–9] Stress urinary incontinence is common in cases of mild pelvic organ prolapse, whereas urgency urinary incontinence, urinary urgency, and voiding symptoms are common in cases of moderate or severe pelvic organ prolapse (Level 3).[1,10,11]

CQ8. How do FLUTS affect sexual function?

Summary: It has been reported that approximately half of women with LUTS present sexual dysfunction, and that LUTS are an independent risk factor for female sexual dysfunction.[12–15] There is a higher rate of sexual dysfunction in OAB with urinary incontinence (OAB-wet) than in OAB-dry, and sexual dysfunction improves with treatment for OAB.[16–19] Stress urinary incontinence is strongly involved in urinary incontinence during sexual intercourse, with reduced urethral resistance contributing the most.[20–23] In surgery for stress urinary incontinence and pelvic organ prolapse, it has been reported that, while it improves sexual function, there is apprehension that transvaginal mesh implantation can cause dyspareunia (coital pain) and chronic pain.[24–30]

CQ11. Is hormone replacement therapy recommended for FLUTS?

Summary: For FLUTS, and in particular various symptoms of OAB, it has been reported that treatment by vaginal administration is more effective than oral therapy (Level 1).[31–34] However, in Japan, there are no vaginal estrogen preparations that are covered by health insurance for OAB[5] (recommendation Grade C1).

CQ12. For female OAB, what is the difference in the effectiveness and safety according to the type of anticholinergic agent and beta-3 agonists?

Summary: The effectiveness of anticholinergics and beta-3 agonists is comparable (Level 1).[35] Beta-3 agonists have few adverse

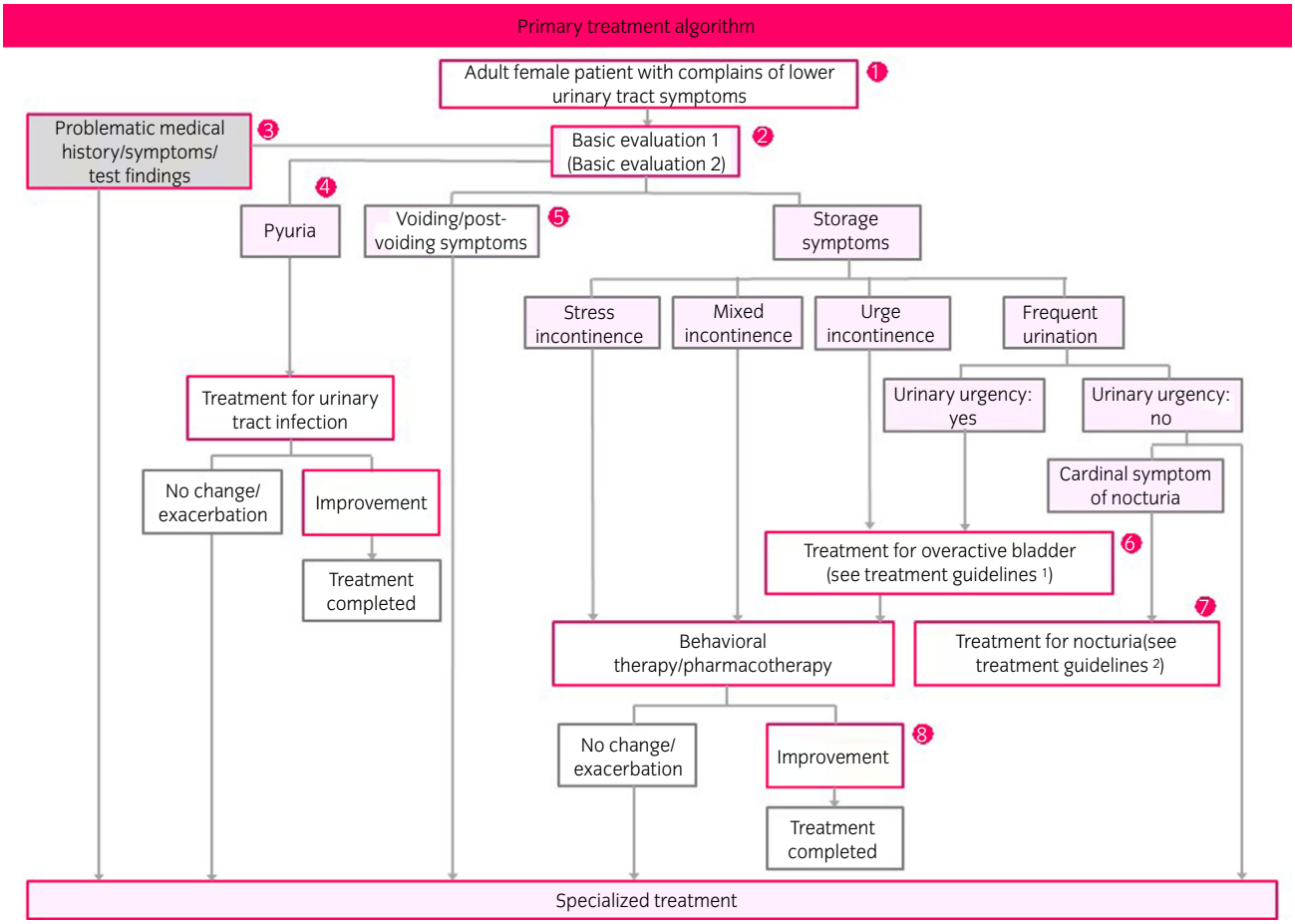

Fig. 1 Primary treatment algorithm. ❶ This algorithm is to be used for adult women complaining of any LUTS (e.g. urinary frequency, nocturia, urinary urgency, urinary incontinence, dysuria, bladder pain). Several diseases and conditions* can cause FLUTS. *Examples include OAB, bacterial cystitis, interstitial cystitis, bladder cancer, bladder calculus, urethritis, urethral stricture, urethral diverticulum, a weakened pelvic floor (e.g. urethral hypermobility, pelvic organ prolapse), complications of surgery of or radiotherapy to the pelvic region, vesicovaginal/urethrovaginal fistula, polyuria, nocturnal polyuria, and various neurological diseases (e.g. neurogenic bladder). ❷ Basic evaluation contains two components: The first, Basic Evaluation 1, is for all patients and includes an interview to discuss the symptoms and medical history, physical findings, and urine analysis of the patient. The second evaluation (Basic Evaluation 2) is for selected patients and includes a symptom/QOL questionnaire-based assessment, bladder diary, residual urine volume measurement, urine cytology, urine culture, serum creatinine measurement, and ultrasound examination. These findings and treatment strategies are explained to the patient to confirm their consent for treatment. ❸ Examination by a specialist (or referral to a specialist) should be considered for patients with problematic medical histories, symptoms, or test findings, including urinary retention, recurrent urinary tract infection, macroscopic hematuria, surgery/ radiotherapy to the pelvic region, neurological disease, lower abdominal distention, reproductive organ abnormalities (ovaries, uterus, vagina, or pudenda), extravaginal prolapse of a pelvic organ, vesicovaginal/urethrovaginal fistula, suggested urethral diverticulum, pyuria with fever, positive urine cytology results, kidney dysfunction, high residual urine volume (≥100 mL), bladder calculus, and abnormal ultrasonographic findings. Examination by a specialist (or referral to a specialist) should also be considered when symptoms are severe or involve bladder or perineal pain. Along with urinary frequency, bladder or perineal pain that intensifies with urine storage in the bladder may be a sign of interstitial cystitis. ❹ Pyuria without fever is treated with antibacterial agents appropriate for urinary tract infections (cystitis). Quinolones are first-line drugs administered to premenopausal women when the causative bacterium is unknown or is known to be a Gram-positive bacterium. If a Gram-negative bacillus has been confirmed via urine analysis, cephems or penicillin/beta-lactamase inhibitor combinations are used. Because Gram-positive bacteria are not typically isolated in postmenopausal women with acute cystitis and because *E. coli* isolates frequently confer quinolone-resistance, cephems or penicillin/beta-lactamase inhibitor combinations are first-line drugs. However, patients should be carefully observed for underlying diseases that may persist even after the infection has been cured. ❺ Examination by a specialist should be considered if voiding and post-voiding abnormalities present as the primary symptoms. Residual urine volume should be measured when the patient has both voiding and storage symptoms. Diagnosis and treatment of storage symptoms should be prioritized if residual volume is <100 mL, and specialist examination should be considered when residual volume is ≥100 mL. ❻ See "Behavioral therapy" and "Drug therapy for OAB" in the main text if OAB symptoms (urinary frequency or incontinence with urinary urgency) are present. The Guidelines for the Diagnosis and Treatment of Overactive Bladder[5] may also be referred to. ❼ If the main symptom is nocturia, nocturnal polyuria or sleep disturbance may be the cause; therefore, the Guidelines for the Diagnosis and Treatment of Nocturia[6] should be consulted. ❽ Symptoms may improve with temporary treatment. Therefore, it is essential to avoid continuing aimless treatment after symptoms have improved and to consider changing or revising the therapeutic plan, including discontinuing or reducing the dose of medications.

reactions based on anticholinergic activity and, in terms of safety, they are superior to anticholinergics (Level 1).[36] It has been reported that different anticholinergics exhibit different effects and, depending on the type, dosage, and formulation type, adverse reactions may occur (Level 1). However, no reports have evaluated the superiority or inferiority of each type.[37,38]

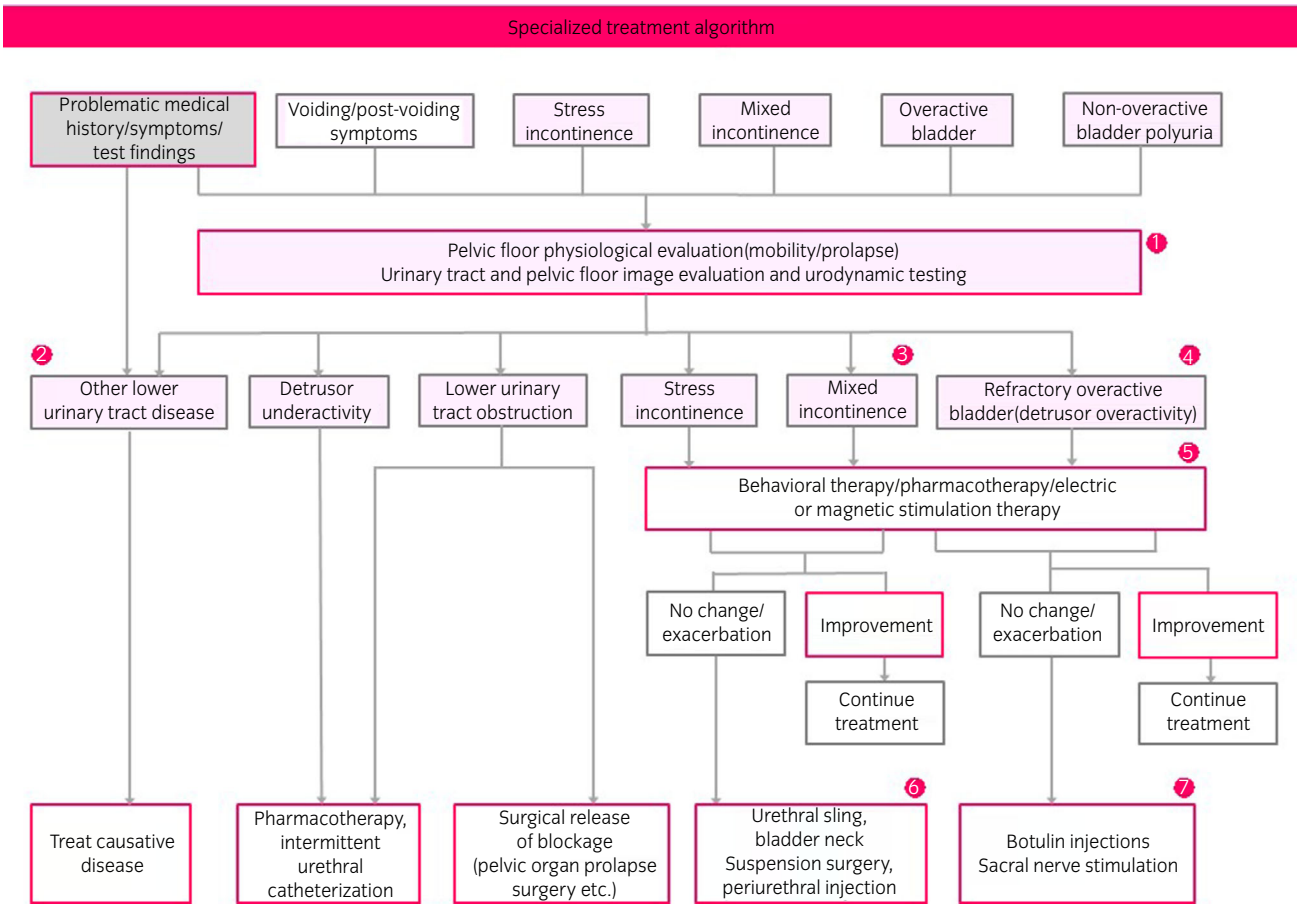

Fig. 2 Specialized treatment algorithm. ❶ Physical evaluation of the pelvic floor should be performed, including abdominal pressure loading, to detect and assess the severity of urethral hypermobility and pelvic organ prolapse. Imaging assessment of the urinary tract and pelvic region and urodynamics measurement should be performed as needed, and these findings and treatment strategies should be explained to the patient to confirm their consent for treatment. ❷ Examples of other lower urinary tract diseases include recurrent urinary tract infection, interstitial cystitis, bladder cancer, bladder calculus, vesicovaginal/urethrovaginal fistula, bladder/urethral diverticulum, neurogenic bladder, and psychogenic urinary frequency. ❸ Mixed incontinence can be stress incontinence-dominant or urgency incontinence- (OAB symptoms) dominant. Generally, treatment should be selected according to the dominant symptoms. ❹ Refractory OAB is defined as OAB unresponsive to behavioral or drug therapies for at least 12 weeks.[1] These patients may show severely reduced bladder capacity and detrusor overactivity when urodynamics is measured. ❺ Specialized behavioral therapy treatment includes lifestyle guidance, bladder training, and pelvic floor muscle training (including biofeedback therapy) performed by a specialist. Drug therapy involves selection and dose adjustment of drugs by a specialist or combination therapies. Neuromodulation therapy can take the form of transvaginally, transanally, or transcutaneously delivered electrical or magnetic stimulation therapy. ❻ Periurethral injection of a bulking agent is indicated for patients with urethral sphincter deficiency; however, there are currently no bulking agents that are approved for use in Japan. ❼ Cystoscopic botulinum toxin injection surgery and sacral nerve stimulation therapy administered via an implanted device are also effective treatments for refractory OAB.

CQ13. Is combination therapy using anticholinergics and beta-3 agonists recommended for female OAB?

Summary: The effectiveness and safety of the anticholinergic solifenacin in combination with the beta-3 agonist mirabegron have been confirmed in trials conducted overseas (Level 1), and therefore, solifenacin and mirabegron combination therapy is recommended when the effects of monotherapy are insufficient[40–43] (recommendation Grade A).

The results for the safety and effectiveness of combination therapy using other anticholinergics with mirabegron have also been reported[44] (recommendation Grade B).

Concurrent therapy using vibegron and anticholinergics has not been fully examined[45,46] (recommendation Grade C1).

CQ14. Do therapeutic drugs for OAB affect cognitive function?

Summary: The effectiveness and safety of anticholinergics have been confirmed (Level 1); however, there are no reports with a high level of evidence about adverse reactions to the central nervous system. While the incidence is low, cases of cognitive dysfunction thought to be caused by the drugs has been reported, and therefore, when administering such drugs, precautions should be taken and monitoring should be conducted.[5,47,48]

The effect of beta-3 agonists on cognitive function in a small number of cases has been reported, and while there was no clear adverse reaction observed, evidence needs to be gathered to draw a conclusion.[49,50]

CQ16. Are anticholinergics and beta-3 agonists recommended for mixed urinary incontinence?

Summary: For urgency incontinence-predominant mixed urinary incontinence, anticholinergics are effective (Level 1;[51–55] recommendation Grade A).

There are no RCTs using beta-3 agonists for mixed urinary incontinence. However, because beta-3 agonists are effective for OAB, it is inferred that they would exhibit the same effectiveness as anticholinergics for mixed urinary incontinence.[56] Further evidence needs to be gathered going forward (Level 5; recommendation Grade C).

CQ23. Is the MUS procedure recommended for mixed urinary incontinence?

Summary: The MUS procedure is effective for stress-predominant mixed urinary incontinence (Level 2;[57–61] recommendation Grade B).

CQ24. Is prophylactic surgery for stress urinary incontinence recommended for urinary incontinence arising after surgery for pelvic organ prolapse?

Summary: Prophylactic surgery for stress urinary incontinence significantly reduces incontinence following surgery for pelvic organ prolapse; however, it increases the postoperative rate of voiding dysfunction and complications, and thus, the risks might be greater than the benefits (Level 1;[62–69] recommendation Grade C2).

Summary of the guidelines

What are FLUTS?

LUTS can be broadly divided into the three types of storage symptoms, voiding symptoms, and post-micturition symptoms. It has been found that FLUTS are associated with sexual function, pregnancy and delivery, and pelvic organ prolapse.[1,70,71] Among women, stress urinary incontinence caused by pelvic floor dysfunction is common, and the chief complaint is primarily storage symptoms.[72,73] Furthermore, nocturia is often attributed to causes other than lower urinary tract dysfunction, that is, nocturnal polyuria and sleep disturbance are often involved, and it is the most frequent symptom among both men and women.[74]

Genitourinary syndrome of menopause is an umbrella term covering various symptoms and syndromes caused by atrophy of the vagina, external genitalia, and lower urinary tract as a result of reduced estrogen following menopause.[75] The primary symptoms of genitourinary syndrome of menopause include dryness, burning sensation, and itchiness of the external genitalia and vagina, with insufficient lubrication and pain during sexual intercourse, and urinary urgency, urination pain, and recurrent urinary tract infection.

The epidemiology of FLUTS

Many middle-aged and elderly women have LUTS,[76–84] and, in Japan, the incidence of LUTS is high with regard to nocturia and increased daytime urinary frequency, followed by reduced urine flow, stress urinary incontinence, urinary urgency, urgency urinary incontinence, feeling of residual urine, and bladder pain in women.[79] Most symptoms increase in frequency with age, and approximately 78% of men and women aged 60 years and older present some kind of LUTS.[79] The incidence of pelvic organ prolapse, which is specifically seen in women, is higher among parous women than nulliparous women, with a higher incidence associated with vaginal delivery when compared to Caesarean section.[85,86]

FLUTS and QOL

Dysfunction of the lower urinary tract causing LUTS is essentially a QOL illness, and to determine the level of severity, treatment selection, and treatment outcomes concerned, it is important to evaluate QOL. Among LUTS, storage symptoms, which are more common in women, tend to have a greater impact on QOL than voiding symptoms and post-micturition symptoms.[1,73,76,79] Symptom/QOL questionnaires with verified validity in Japanese have been used in clinical practice and in studies regarding urinary incontinence, OAB, nocturia, pelvic organ prolapse, and female sexual function.[1,71,87–92]

There are various illness-specific QOL questionnaires for various types of LUTS and illnesses. Questionnaires for urinary incontinence in general include the Urogenital Distress Inventory, the IIQ, the I-QOL, the KHQ, and the ICIQ-SF.[1] For OAB, the aforementioned questionnaires for urinary incontinence in general are used as well as the OAB-q[90] and for nocturia, the nocturia-specific QOL questionnaire, the N-QOL, is used.[91]

Given that the questionnaires above primarily focus on storage symptoms, the IPSS, and related QOL score (IPSS-QOL), and the CLSS are questionnaires of symptoms including storage, voiding and post-micturition symptoms and they contain questions pertaining to QOL.[73,87–89] The IPSS is considered useful for the evaluation of FLUTS, and it is also used for the evaluation of LUTS accompanied by pelvic organ prolapse. Questionnaires developed in Japan include the OABSS[5,92] and the CLSS.[87–89]

Pathology and illness

LUTS onset in middle-aged and elderly women involves pregnancy, delivery, pelvic organ prolapse, menopause, estrogen deficiency, neurologic disorders, and aging.[1,5,6,75] Causative diseases with a high incidence of storage symptoms include urinary tract infection, OAB, stress urinary incontinence, pelvic organ prolapse, and interstitial cystitis,[1,93–98] whereas causes of voiding symptoms and post-micturition symptoms include organic disease of the lower urinary tract such as bladder neck obstruction, bladder calculus, and

urethral stricture, as well as age-related underactive bladder, disorders of the central nervous system, neurogenic bladder (seen following surgery for uterine cancer and rectal cancer), a history of urinary incontinence surgery, and cases associated with pelvic organ prolapse.[1,9,99–104] Diagnosis is difficult in instances that cannot be inferred based on the patient's medical history, and urodynamic measurement is performed as needed in such cases.

Diagnosis

Evaluations that are necessary for the diagnosis of FLUTS (Basic Evaluation 1) include medical interview of patient symptoms and medical history, examination of physical findings, and performing urine analysis. Evaluations that should be performed on selected cases (Basic Evaluation 2) include evaluation with symptom/QOL questionnaires, bladder diary, residual urine measurement, urine cytology, urine culture, serum creatinine measurement, and ultrasonography (refer to the algorithm for primary treatment). These findings and the treatment policy will be explained to the patient, and the patient's wishes with regard to treatment will be confirmed.

Symptoms and questionnaires

To evaluate symptoms and QOL, the use of a questionnaire with confirmed validity is recommended. For the questionnaire evaluating the CLSS with QOL, it is useful to determine all FLUTS without exception including urinary incontinence and bladder pain and to evaluate QOL (Table 2).[1,87–89]

Illness (urinary incontinence)-specific symptoms and QOL questionnaires available in Japanese and for which validity has been confirmed include the ICIQ-SF, the KHQ, the IIQ, and the I-QOL.[1] Questionnaires in Japanese that evaluate OAB include the OAB-q and OABSS.[1,5] For nocturia, there is the N-QOL,[6] while for interstitial cystitis, there is the Interstitial Cystitis Symptom Index, the Interstitial Cystitis Problem Index, and the Pain Urgency Frequency scale.[1]

Bladder diary

A bladder diary is useful in the event of increased daytime urinary frequency, nocturia, and urinary incontinence. It is also useful to determine whether these symptoms are caused by decreased volume per urination, by (nocturnal) polyuria, or by both combined.[1,5,6] The survey period should last from 3 days to approximately 1 week.[1,6,105,106] The following items can be measured from the bladder diary: daytime urinary frequency, nocturia, 24-h frequency, 24-h urine output (24-h production), maximum voided volume, nocturnal urine volume, and nocturnal polyuria index (nocturnal polyuria index = nocturnal urine volume/24-h urine volume). Nocturnal polyuria is diagnosed when the nocturnal polyuria index is ≥0.2 (young adults) or ≥0.33 (individuals ≥65 years).[1,6] It has also been reported that nocturnal polyuria is diagnosed when nocturnal urine output is ≥10 mL/body weight in kg.[107]

Medical examination

As per normal urologic medical examinations, findings associated with LUTS in general, as well as the presence or absence of any neurologic illness, gynecologic illness, or

Table 2 CLSS questionnaire

Please circle the number that applies best to your urinary condition during the last week				
	0	1	2	3
Q1: How many times do you typically urinate from waking in the morning until going to sleep at night?	0–7	8–9	10–14	15+
Q2: How many times do you typically urinate from going to sleep at night until waking in the morning?	0	1	2–3	4+
How often do you have the following symptoms?	Never	Rarely	Sometimes	Often
Q3: A sudden strong desire to urinate, which is difficult to postpone	0	1	2	3
Q4: Leaking of urine because you cannot hold it in	0	1	2	3
Q5: Leaking of urine when you cough, sneeze, or strain	0	1	2	3
Q6: Slow urinary stream	0	1	2	3
Q7: Need to strain when urinating	0	1	2	3
Q8: Feeling of incomplete emptying of the bladder after passing urine	0	1	2	3
Q9: Pain in the bladder	0	1	2	3
Q10: Pain in the urethra	0	1	2	3

CLSS (sum of Q1–10)

From symptoms 1–10, please circle the number corresponding to no more than three symptoms you find bothersome.

Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Not applicable

Of the symptoms you chose above, please circle the number of the symptoms that you find most bothersome (one only).

Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Not applicable

If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?

Delighted	Pleased	Mostly satisfied	About equally satisfied and dissatisfied	Mostly dissatisfied	Unhappy	Terrible
0	1	2	3	4	5	6

congenital abnormalities are examined. Distension of the mid-lower abdomen region suggests that the bladder is enlarged because of a large volume of residual urine, and in the event that a depression, new hair growth, and fatty deposition are observed in the midline of the buttocks, the subject might have spina bifida.[1]

Patients are evaluated by visual examination and internal examination in the lithotomy position as required. Examination is performed to determine the presence or absence of an abnormality of the external urethral opening such as urethral caruncle or urethral stricture, as well as the presence of any redness or atrophy of the vagina. Urethral diverticulum is determined when a bulge is palpated at the anterior wall of the proximal vagina and an opaque discharge from the urethral opening is observed upon applying pressure. When stress urinary incontinence is suspected, evaluate the presence or absence of urethral hypermobility. Evaluation is easily achieved by performing the Q-tip test. The stress test is also a means of verifying the presence or absence of actual urinary incontinence.[1]

Moreover, the presence or absence of pelvic organ prolapse such as cystocele, uterine prolapse, and rectocele is to be evaluated. In doing so, changes in sagging caused by abdominal pressure should also be evaluated. Applying pressure to the anterior and posterior walls of the vagina as needed makes observation of rectocele and cystocele easier, respectively. Pelvic organ prolapse should be evaluated and described using the Pelvic Organ Prolapse Quantification system.[1]

In the event that urinary incontinence without dry time is observed, bladder (ureteral) vaginal fistula and ectopic ureteral opening should be suspected. Vaginal observation with bladder infusion of physiological saline containing indigo carmine may be useful. In rectal examinations, the amount of fecal loading and the presence or absence of findings that affect voiding should be examined. When the anal tonus is reduced, peripheral nerve damage in the sacral region of the spinal cord (S3–5) is suspected, and if such damage has progressed, the nerves above the sacral region of the spinal cord may be damaged.[1]

Tests

1. Urine analysis
   Urine analysis is a useful test to differentiate illnesses such as urinary tract infection, urinary tract stones, bladder cancer, and diabetes mellitus. The test is performed as a basic investigation for all patients.[1]
2. Residual urine measurement
   Measurement by transabdominal ultrasound is generally noninvasive. If residual urine is ≥100 mL, then consider specialized treatment. Before commencing treatment with anticholinergics, it is recommended that residual urine be measured.[1]
3. Serum creatinine measurement
   Serum creatinine is to be measured in selected patients.
4. Ultrasonography
   Ultrasonography enables information to be obtained regarding residual urine volume, the bladder shape, bladder tumors, and bladder calculus. For image evaluation of the pelvic floor and urethra, transperineal or transvaginal ultrasonography is used.[1]
5. Pad test
   The pad test is indicated for patients in whom urinary incontinence is indicated by medical history taking. The test serves as an objective indication of the severity of urinary incontinence, and a 1-h pad test can be used. The 24-h pad test is used to find the volume of incontinence over a 24-h period in everyday life, and while it is more suitable than the primary diagnosis to determine the therapeutic outcomes, there are no established reference values for making judgments.[108]
6. Urodynamics measurement
   Urodynamics measurement is useful for elucidating a patient's condition; however, it is not necessarily required for diagnosis and starting treatment.[1] The primary investigations include uroflowmetry, cystometry, urethral pressure profile, and abdominal leak point pressure.
   Cystometry often reveals findings of poorly compliant bladder in neurogenic bladder caused by sequelae following pelvic surgery and radiotherapy such as for uterine cancer or rectal cancer and, in diabetes-related neurogenic bladder, detrusor underactivity is often found.[109] When the maximum urethral closure pressure is <20–30 cmH_2O, and if the abdominal leak point pressure is <60 cmH_2O, urethral sphincter deficiency should be suspected.[110–113]
   A pressure flow study is also useful for evaluating the pathology of voiding disorders. At this point in time, however, there are no clear diagnostic criteria for lower urinary tract obstruction in women.[114–117] Several criteria have been proposed, such as $P_{det}Q_{max} > 2 \times Q_{max}$[114] and $P_{det}Q_{max} > 1.5 \times Q_{max} + 10$,[115] with the range generally defined as Q_{max} <12–15 mL/s and P_{det} >20–40 cmH_2O.[116]
7. Endoscopy (bladder and urethral endoscopy)
   Endoscopy enables the presence or absence of bladder trabeculation, bladder diverticulum, interstitial cystitis, bladder/urethral vaginal fistula, urethral stenosis, urethral diverticulum, bladder calculus, and bladder tumors to be identified. Furthermore, in the event that the patient has a history of surgery for urinary incontinence and pelvic organ prolapse, on occasion, bladder mesh exposure occurs. In typical cases of interstitial cystitis, increased vascularization in the bladder wall, Hunner's lesions, and petechial bleeding are observed.[118]
8. Chain cystourethrogram
   In patients with stress urinary incontinence, the bladder neck is often dilated, and on lateral view images, the angle formed by the posterior surface of the bladder and the urethra (posterior vesicourethral angle) is often open.[1] Extrapelvic sagging of the bladder (cystocele) is also observed.
9. Other examinations
   Voiding cystourethrogram is useful for the diagnosis of urethral stricture, vesicoureteral reflux and urethral diverticulum.
   Image diagnosis of the upper urinary tract is first performed by ultrasound examination. If the patient has a history of hematuria, urinary tract stones, or urothelial

cancers, computed tomography urography and intravenous pyelogram can serve as an option.[119] Nuclear magnetic resonance imaging has high contrast resolution for soft tissue and is excellent for delineating the female reproductive organs and pelvic floor. In recent years, attempts have been made using cine magnetic resonance imaging to observe the movement of the pelvic floor when abdominal pressure is applied for patients with stress urinary incontinence and pelvic organ prolapse.[120]

Treatment

Behavioral therapy

Behavioral therapy for FLUTS includes lifestyle interventions, PFMT, bladder training, scheduled voiding regimens, and other conservative treatments (Table 3).

1. Lifestyle interventions
   It has been found that OAB and stress urinary incontinence involve various lifestyle factors including obesity, smoking, and excessive fluid intake (carbonated drinks and alcohol), and it is recommended that patients improve various lifestyle habits. However, in a large-scale RCT, the efficacy of such improvement was only seen with weight loss (Level 1).[1]
   a. Weight loss: Recommendation Grade A
      Several reports have indicated that weight gain and body mass index correlate with urinary incontinence, and that, compared to controls, weight loss through diet with exercise therapy significantly reduces urinary incontinence (Level 1).[1,121–125]
   b. Physical activity: Recommendation Grade C1
      It has been suggested that moderate exercise reduces the risk of urinary incontinence onset; however, there is insufficient evidence to support this (Level 4).[1,126–130] Since 2011, there have been reports in women, in general, women with obesity and diabetes, and frail women. However, there have been no large-scale RCTs.[126–130]
   c. Cessation of smoking: Recommendation Grade C1
      It has been reported that smoking can increase the risk of severe incontinence, and experimentally, that nicotine causes bladder contraction.[1] Some reports indicate that urinary incontinence is common in smokers.[126,131,132] However, no RCTs have been conducted to investigate the effectiveness of smoking cessation (Level 4).
   d. Limitation of fluid intake (including alcohol and carbonated drinks): Recommendation Grade C1
      Several reports have described the relationship of the amount of fluid intake, alcohol, and carbonated drinks with LUTS and urinary incontinence; however, there is no clear evidence with regard to improving OAB and urinary incontinence by limiting fluid intake and caffeine intake (Level 4).[1,133–142] Guidance on fluid intake is often performed along with other behavioral therapies.
   e. Ameliorating constipation: Recommendation Grade C1
      The relationship between defecation disorder (constipation and fecal incontinence) and LUTS has been reported. Although it has also been reported that straining to defecate can be a risk factor for stress urinary incontinence and urinary urgency, and there is no evidence regarding the effectiveness of improving constipation (Level 4).[1]
2. PFMT
   a. PFMT: Recommendation Grade A
      PFMT is the first choice of treatment for urinary incontinence in women. There are various methods of PFMT, which differ according to the type of urinary incontinence targeted, the presence or absence of concurrent therapy, treatment duration, and evaluation method reported; however, most RCTs support the case that PFMT is effective for stress urinary incontinence, and it is also effective for urgency and mixed urinary incontinence.[1,143–151] Furthermore, there are many reports of RCTs supporting the effectiveness of methods combining various treatment methods such as biofeedback training and bladder training (Level 1).[1]
   b. The effect of PFMT during pregnancy and postpartum to prevent urinary incontinence: Recommendation Grade B
      For women with urinary incontinence, PFMT can prevent exacerbation. However, it has been reported that when including women without urinary incontinence, no superiority has been demonstrated compared to controls (Level 1).[1,152–159]
   c. Feedback and biofeedback training: Recommendation Grade B
      Various small-scale RCTs have provided grounds supporting the effectiveness of this training (Level 2).[1,160–165]
3. Bladder training and scheduled voiding regimens: Recommendation Grade B
   Bladder training is a method that improves storage symptoms by holding on to urine. Broadly speaking, bladder training involves scheduled voiding regimens, combined with timed voiding and prompted voiding.[1,3,166–169] Bladder training is performed for OAB, with high efficacy that is comparable to that of anticholinergics (Level

Table 3 Behavioral therapy

Therapeutic method	Grade of recommendation
Lifestyle interventions	
Weight loss	A
Exercise	C1
Cessation of smoking	C1
Diet (fluid consumption) intervention	C1
Management of constipation	C1
Pelvic floor muscle training	A
Bladder training/Scheduled voiding regimens	B
Miscellaneous	
Vaginal cone	C1
Acupuncture	C1
Thermal sheet	C1 (not yet approved)
Hypnotherapy	Pending (not yet approved)

2).[1,166,167] Although it is also reported to be effective for mixed and stress urinary incontinence, there is insufficient evidence to support this (Level 2).[1]

4. Other conservative treatments
   a. Vaginal cone: Recommendation Grade C1
      There is no superiority observed for vaginal cone treatment compared to PFMT (Level 2).[1]
   b. Acupuncture: Recommendation Grade C1
      The effectiveness of acupuncture for FLUTS has not been fully demonstrated (Level 3).[170–172] With regard to RCTs of acupuncture therapy for OAB in women, only a small subject sample has been reported prior to 2010. An RCT comparing acupuncture therapy with placebo acupuncture therapy in 74 patients revealed that the frequency of urinary incontinence increased in both groups and no significant difference was observed. A significant improvement compared to the control group, however, was found for increased bladder capacity, urinary urgency, urinary frequency, and QOL scores.[172]
   c. Steam thermopatch: Recommendation Grade C1 (off-label)
      The effectiveness of steam thermopatch treatment for FLUTS has not been fully demonstrated (Level 2).[173]
   d. Hypnotherapy: Recommendation grade to be determined
      The effectiveness of hypnotherapy for FLUTS has not been fully demonstrated (Level 3).[1,174]

Drug therapy

This chapter explains the efficacy and safety of drug therapy for FLUTS, focusing on drug therapy for OAB and stress urinary incontinence, for which evidence has been accumulated. We also outline drugs that are experimentally used when treating voiding disorder seen in neurogenic bladder.

1. Drug therapy for OAB
   Drug therapy serves as the basis for the treatment of OAB (Table 4). Drugs for which the efficacy and safety have been examined include anticholinergics and beta-3 adrenoceptor agonists (beta-3 agonists). Furthermore, evidence has been accumulated for the effectiveness of treatment by botulinum toxin injection in the bladder wall for refractory OAB; however, at the time of publishing this guideline, the treatment had not yet been approved for health insurance (approved in April 2020 in Japan).
   a. Anticholinergics
      At present, anticholinergics are the most common drug used for the treatment of OAB, and their effectiveness and safety have been demonstrated. However, when using anticholinergics, due care should be paid to adverse reactions caused by muscarinic receptor agonists.
      (1) Oxybutynin: Recommendation Grade B
          Oxybutynin has an antimuscarinic action as well as a direct relaxation effect and paralysis effect on smooth muscles. This agent has been examined in many clinical studies, and its effectiveness has been fully demonstrated (Level 1).[1] However, the incidence of adverse reactions related to antimuscarinic action is higher compared to other anticholinergics (Level 1), and it is possible that this agent causes adverse reactions of the central nervous system (such as

Table 4 Therapeutic drugs for OAB (urinary frequency and urinary incontinence)

Generic name	Administration and dosage	Grade of recommendation
Anticholinergic drug		
Oxybutynin	2–3 mg, 3 times/day, orally	B
Oxybutynin patch	Application of a single patch (containing oxybutynin 73.5 mg/patch) once daily	A
Propiverine	20 mg once daily, orally. Can be increased to 20 mg twice daily	A
Tolterodine	4 mg once daily, orally. Can be increased to 10 mg daily	A
Solifenacin	5 mg once daily, orally. Can be increased to 10 mg daily	A
Imidafenacin	0.2 mg/dose twice daily administered orally after breakfast and supper. Can be increased to 0.2 mg twice daily	A
Fesoterodine	4 mg once daily, orally. Can be increased to 8 mg/day	A
Propantheline	One tablet (15 mg) 3–4 times daily in adults, administered orally	C1
β3-Adrenergic receptor agonist		
Mirabegron	50 mg once daily after meal, orally	A
Vibegron	50 mg once daily after meal, orally	A
Flavoxate	200 mg per dose, 3 times/day orally	C1
Tricyclic antidepressants (such as imipramine)	Indicated for pediatric nocturia	C1
Kampo formulation (goshajinkigan)	7.5 g/day, administered in 2–3 portions	C1
Estrogen	–	C1
Botulinum toxin	–	Pending (not approved at the time of guideline publication and approved in April 2020 in Japan)
Antidiuretic hormone (desmopressin)	Indicated for pediatric nocturia and nocturia due to nocturnal polyuria in male	Pending (not yet approved for nocturia in females in Japan)
Alpha-adrenoreceptor blockers	–	Pending (not yet approved)

cognitive disturbance) via the blood–brain barrier, and thus, caution should be exercised when using oxybutynin in elderly patients in particular.[175–177]

(2) Oxybutynin patch: Recommendation Grade A
Oxybutynin patch is the first percutaneous absorption-type drug used to treat OAB in Japan. Based on trials in Japan, it has been reported to be effective for various symptoms of OAB, with few adverse reactions compared to oral anticholinergics (Level 1).[1,178] However, due care should be paid to skin reactions at the attachment site.[178]

(3) Propiverine: Recommendation Grade A
Propiverine is a drug that has an antimuscarinic action and calcium antagonistic action. Large-scale RCTs comparing this agent against a placebo and other agents have been conducted primarily overseas, and it has been reported that propiverine is effective against OAB symptoms, with few adverse reactions (Level 1).[1,179]
In Japan, administration is set at 20 mg per day (given in one or two doses).[179–181] Up to 40 mg per day may be administered under health insurance coverage.

(4) Tolterodine: Recommendation Grade A
Tolterodine has been found to have no selectivity to subtypes of muscarinic receptors, with high transferability and binding affinity to bladder tissue, and higher selectivity for the bladder than the salivary glands. A dose of 4 mg given once per day has been found to improve various symptoms of OAB and to improve QOL. Moreover, it is an agent found to be effective and safe for patients including elderly patients with OAB and patients with severe OAB (Level 1).[1,182]

(5) Solifenacin: Recommendation Grade A
Solifenacin is an anticholinergic agent that was invented and developed in Japan. It has been confirmed to be an agent with relatively high affinity to the muscarinic receptor M3 and greater selectivity for the bladder than the salivary glands. It has been found to improve the sense of urinary urgency, increased urinary frequency, urgency urinary incontinence, and nocturia in OAB (Level 1).[1,183,184] Its effectiveness has also been confirmed for elderly patients and severe patients (Level 1), and it has been reported to have little impact on cognitive function (Level 2).[183]

(6) Imidafenacin: Recommendation Grade A
Imidafenacin is an anticholinergic agent that was invented and developed in Japan. It is an agent with high selectivity to the muscarinic receptors M3 and M1, with high selectivity for the bladder compared to the salivary glands. Among the agents approved to date, it has a short half-life (2.9 h).[1] It has been found to effectively improve the sense of urinary urgency, increased urinary frequency, and urgency urinary incontinence, with few adverse reactions (Level 1). The effectiveness for nocturia (Level 2) and sleep disturbance (Level 4) has been demonstrated. It has been reported to have a low rate of transition to dementia in patients with mild cognitive impairment (Level 3).[1,185,186]

(7) Fesoterodine: Recommendation Grade A
Fesoterodine is not selective for muscarinic receptor subtypes, but its active metabolites (5-hydroxymethyl tolterodine) show the same effectiveness and safety as tolterodine for various symptoms of OAB (Level 1).[1,187] Furthermore, it is reported to be effective for elderly patients with OAB and frail elderly patients with OAB (Level 1).[188–190]

b. Beta-3 adrenoceptor agonists
In the storage phase, sympathetic nerve activity is predominant, and beta-adrenoceptor agonists (beta-agonists) in smooth muscles of the bladder relax the bladder. These beta receptors are classified into three types, beta-1, beta-2 and beta-3, and in the human bladder, beta-3 receptors account for 97%.[1] Beta-3 agonists exhibit the same efficacy as anticholinergics without exhibiting the adverse reactions based on the anticholinergic action. At present, the two types used are mirabegron and vibegron.

(1) Mirabegron: Recommendation Grade A
Mirabegron, which was invented and developed in Japan, is the first beta-3 adrenoceptor agonist (beta-3 agonist) made available worldwide.[1] Clinical research in Japan and overseas has demonstrated the effectiveness and safety of mirabegron[191,192] (level). Trials of combination therapy using mirabegron at a dose of 50 mg with other types of anticholinergics (solifenacin at 5 mg, propiverine at 20 mg, imidafenacin at 0.2 mg, and tolterodine at 4 mg) have shown that in all combination therapy groups, a significant improvement was found compared to baseline.[40,42,44,198–200]

(2) Vibegron: Recommendation Grade A
Vibegron is a novel beta-3 adrenoceptor agonist (beta-3 agonist) that was made commercially available in 2018 after undergoing a phase III trial for the first time worldwide in Japan.[193] The approved dosage in Japan for this agent is 50 mg, and a single dose per day is effective for various symptoms of OAB, with mild adverse reactions.[45,193] Furthermore, this agent has not been found to have an inhibitory action nor induction effect for CYP enzymes, and therefore, almost no drug interaction is seen. Moreover, it is a drug that does not require dose adjustment due to liver function and kidney dysfunction.[45,193,194]

c. Estrogen: Recommendation Grade C1
Estrogen has been experimentally used for many years in the treatment of the sense of urinary urgency and urgency incontinence.[1,2] In recent years, several RCTs have been performed that have demonstrated the effectiveness of estrogen.[1,195,196] Treatment includes oral therapy and local administration (vaginal). The effectiveness of local administration in particular has been confirmed (Level 1).[1,195]

d. Botulinum toxin: Recommendation grade to be determined (off-label, covered by health insurance from April 2020)
It has been found that botulinum toxin inhibits the release of acetylcholine from cholinergic nerves and acts on afferent nerves via chemical denervation.[1] Evidence is being gathered with regard to the efficacy and safety of infusion therapy of this agent in the bladder wall. It is an effective treatment method for patients with neurogenic and idiopathic OAB who are ineligible for oral therapy (Level 1).[1,197–200]

2. Drug therapy for stress urinary incontinence
Drugs are selected to improve reduced urethral closure pressure during storage.

a. Beta-2 adrenoceptor agonist (clenbuterol): Recommendation Grade B
Although this agent is used as a therapeutic drug such as for bronchial asthma, it increases contraction of the external urethral sphincter muscle (Level 2).[1] In Japan, it is covered by health insurance for stress urinary incontinence.

b. Chinese medicines (*Hochu-ekki-to* and plant extracts): Recommendation Grade C1
There is insufficient evidence to support the effectiveness of Chinese medicine. It has been reported that *Hochu-ekki-to* (Buzhongyiqitang) as well as processed foods containing summer squash seed extract and soybean germ extract for medical purposes are effective for female stress urinary incontinence (Level 4).[1]

c. Tricyclic antidepressants: Recommendation Grade C2
Imipramine, amitriptyline and clomipramine are first-generation antidepressants and are covered by health insurance for childhood bed wetting. The evidence supporting their effectiveness for stress urinary incontinence is insufficient (Level 4).[1]

d. Estrogen: Recommendation Grade C2
Reports can be found to suggest the effectiveness of estrogen; however, all of these reports are of small-scale case series and not of randomized, blinded trials. Recent reports indicate that estrogen is not effective for stress urinary incontinence (Level 1).[1] Furthermore, different types of estrogen preparation and various doses used complicate problems.

e. Alpha-adrenoceptor agonists: Recommendation grade to be determined (off-label)
Sympathetic nerve alpha-adrenoceptor agonists cause the urethral smooth muscle to contract and increase urethral resistance.[1] While it is not covered by health insurance in Japan for stress urinary incontinence, it has been used experimentally in the past (Level 4).

f. Duloxetine: Recommendation grade to be determined (off-label)
Duloxetine is a serotonin/noradrenaline reuptake inhibitor, which, based on animal experiments, significantly increases sphincter activity during storage.[1] In Japan, it is not covered by health insurance for stress urinary incontinence; however, it is commercially available as an antidepressant. In Europe, it has been approved for stress urinary incontinence. According to reports overseas, it has been shown to significantly reduce the frequency of urinary incontinence in stress urinary incontinence and to improve QOL (Level 1). Furthermore, the effectiveness of concurrent therapy using this agent and PFMT has been pointed out (Level 2). Associated adverse reactions include gastrointestinal disturbance (nausea, constipation and diarrhea), headache, and dizziness, as well as serious adverse events including serotonin syndrome and neuroleptic malignant syndrome.

3. Drug therapy for voiding dysfunction
Drugs that increase the contractile strength of the detrusor muscle and drugs that reduce urethral resistance can be used. Alpha-adrenoceptor antagonists reduce urethral resistance; however, most drugs are covered by health insurance for voiding impairment associated with prostatic hyperplasia. Therefore, drugs that can be used for women are limited.

a. Drugs that increase contractile force of the detrusor muscle

(1) Bethanechol: Recommendation Grade C1
Bethanechol is one drug that mimics acetylcholine, and the strength of the contractile action of similar drugs on the detrusor smooth muscle in healthy bladder is reported to be: carbachol >acetylcholine >bethanechol >propynylcholine. Because it is harder to degrade bethanechol by acetylcholinesterase than acetylcholine, it can be used in clinical practice (Level 3).[1]

(2) Distigmine: Recommendation Grade C1
Distigmine has the effect of increasing the action of acetylcholine by inhibiting cholinesterase. Distigmine is long-acting at 12–24 h and is used in patients with neurogenic bladder causing reduced contractile force of the detrusor muscle (Level 3).[1]

b. Drugs that reduce urethral resistance
Alpha-adrenoceptor antagonists reduce urethral resistance.

(1) Urapidil: Recommendation Grade B
In Japan, urapidil is the only alpha-adrenoceptor antagonist that can be used for women. In the past, urapidil was used as a hypotensive drug, but it was used to treat prostatic hyperplasia in 1995 and to treat voiding impairment in cases with neurogenic bladder in 1999 (Level 2). Although urapidil does not show selectivity for alpha-1 receptor subtypes, compared to other alpha-adrenoceptor antagonists, it is said to exhibit a more potent alpha-2 receptor antagonist action.[1]

Neuromodulation

Neuromodulation includes pelvic floor ES therapy, interferential low frequency therapy, magnetic stimulation therapy, and sacral nerve ES with an implanted device.

1. ES: Recommendation Grade B
   ES therapy is effective for urgency and stress urinary incontinence.[1] Various RCTs on ES used concurrently with sham stimulation, PFMT, biofeedback training, drug therapy, or these combined have been conducted.[1,196,201–203] There are no large-scale RCTs, and there are no established methods, for example, with regard to the stimulation conditions (Level 2).
2. Magnetic stimulation: Recommendation Grade A
   As per the mechanism for ES, stimulation can be performed with the patient fully clothed. Several RCTs of sham stimulation for urgency and stress urinary incontinence have been reported.[1,204–206] In Japan, magnetic stimulation is covered by health insurance for adult women with OAB accompanied with drug therapy-resistant urinary incontinence (or when drugs cannot be used; Level 1).
3. SNM: Recommendation Grade B
   The effectiveness and long-term therapeutic outcomes of SNM have been reported.[1] In Japan, SNM is covered by health insurance for refractory OAB (Level 2).
   Several RCTs have been reported since 2011. An RCT of 147 patients with OAB, who were allocated to an SNM group or a drug therapy group (anticholinergics) and treated for 6 months, showed that treatment success rate was significantly higher in the SNM group (61% *vs* 42%).[207] In a comparison of surgical botulinum toxin bladder injection (192 patients) and SNM (189 patients; ROSETTA trial), a significant decrease in the frequency of urinary incontinence was observed in the former group after 6 months (−3.9 times *vs* −3.3 times; $P = 0.01$), and a significant improvement in OAB-q short-form scores was observed. Although there was no difference found in terms of convenience, adverse events, or risks, there were more cases of urinary tract infection in the former group.[208] Comparison of the two groups after 2 years showed that the reduction in the frequency of urinary incontinence was unchanged (−3.88 times *vs* −3.5 times), and the group given a botulinum toxin bladder injection had a higher level of satisfaction and greater tolerance to treatment. However, there were more instances of urinary tract infection, and 6% of the cases required self-catheterization.[209]
4. Posterior tibial nerve stimulation: Recommendation grade to be determined (off-label)
   In Europe and the USA, there are grounds to support the effectiveness of posterior tibial nerve stimulation for OAB based on a large-scale RCT (Level 1), and in Japan, it is not covered by health insurance.[1]
   In 2018, a systematic review (including male and neurogenic bladder) of 10 RCTs and three prospective trials showed that, in comparison with a sham treatment (two studies), a significant improvement was found in the ICIQ (–3.7 points), while comparison with anticholinergics (four studies) revealed comparable effects. Moreover, comparison with behavioral therapy (two studies) revealed a significant improvement, with a response rate of 48–93% and a cure rate of 25–45%.[210]

Surgical treatment

1. Procedures for stress urinary incontinence (Table 5)
   Surgical treatment for stress urinary incontinence can be considered when the effects of behavioral therapy and drug therapy are inadequate. In general, surgery is indicated for moderate to severe cases; however, in mild cases also, if patients experience urine leakage during exercise, emphasis is placed on the patient's wishes.
   The standard surgical procedure is MUS placement such as TVT surgery and TOT surgery.[1] Good therapeutic outcomes have been achieved with open abdominal retropubic colposuspension (primarily the Burch procedure). Although all procedures are relatively minimally invasive, fully-informed consent including the possibility of complications is required.
   a. MUS procedure
      (1) TVT surgery: Recommendation Grade A
      The short-term objective success rate of TVT surgery is 80–90% and the mid-term outcomes are also good, at 80%, indicating a high level of patient satisfaction (Level 1).[1,211] Intraoperative bladder perforation occurs in approximately 5% of cases.[212] While the outcomes are comparable to those of TOT surgery, it has been reported that the incidence of postoperative voiding difficulty is high.[1,211,212] Upon comparing the vagina-to-suprapubic (bottom-to-top) and suprapubic-to-vagina (top-to-bottom) approaches, the former has a higher subjective success rate, with lower rate of voiding difficulty, bladder perforation, and vaginal wall erosion caused by the tape.[212]
      (2) TOT surgery: Recommendation Grade A
      The short-term objective success rate of TOT surgery is 80–90%, and the subjective success rate is also good, at 90%, indicating a high level of patient satisfaction, and it has been reported that while outcomes are comparable to those of TVT surgery (Level 1), the

Table 5 Main surgical procedures for stress urinary incontinence

Therapeutic method	Grade of recommendation
Tension-free vaginal tape	A
Transobturator tape	A
Single-incision mini-sling	Pending (not yet approved)
Fascial suburethral sling	A
Open abdominal retropubic colposuspension	A
Laparoscopic retropubic colposuspension	B
Anterior colporrhaphy	D
Needle bladder neck suspension	D
Periurethral injection of bulking agent	Pending (not yet approved)
Artificial urinary sphincter	C1 (not yet approved)

objective success rate is somewhat inferior to that of TVT surgery (Level 2).[1,211,213] Serious complications are rare, and compared to TVT surgery, there are fewer cases of bladder perforation and voiding difficulty, as well as a lower volume of blood loss. It is possible that pain persists after surgery.[1,212]

(3) Single-incision mini-sling surgery: Recommendation grade to be determined (off-label)
In recent years, it has been reported that the short-term outcomes of single-incision mini-sling are comparable to those of MUS procedures (Level 2);[214] however, many reports indicate that the subjective success rate and objective success rate are both low.[1,215,216]

- The therapeutic outcomes of MUS procedures in patients with urethral sphincter deficiency
It has been reported that the therapeutic outcomes of patients with intrinsic urethral sphincter deficiency are lower for both TVT surgery and TOT surgery compared to those of patients without it, and that the therapeutic outcomes are comparable or slightly inferior for TOT surgery *vs* TVT surgery.[1]
- The therapeutic outcomes of MUS procedures for patients with mixed urinary incontinence
The therapeutic outcomes for the stress incontinence component of mixed urinary incontinence are comparable to the effects for patients with stress urinary incontinence alone. In the event of stress-predominant mixed urinary incontinence, the sense of urinary urgency and urge incontinence disappear or improve in over 50% of patients.[1,57,60] The cure rate is higher in patients with stress-predominant incontinence than in other patients.[1]
- The therapeutic outcomes of surgery for stress urinary incontinence performed simultaneously with pelvic organ prolapse repair
For patients with pelvic organ prolapse and stress urinary incontinence, performing prolapse repair at the same time has no significant impact on the outcomes of urinary incontinence surgery.[1] While there are advantages to being able to treat both at one stage, it can result in postoperative voiding difficulty.[1,67–69,217]

b. Fascial suburethral sling: Recommendation Grade A
The therapeutic outcomes are comparable to those of MUS procedures and retropubic colposuspension; however, the operative duration and hospital stay are longer, and it carries a higher incidence of voiding difficulty and urinary tract infection (Level 1).[1,218–220] Fascial suburethral sling is also indicated for patients with urethral sphincter deficiency.

c. Open abdominal retropubic colposuspension: Recommendation Grade A
The general procedure used is the Burch procedure (or modified Burch procedure), with good objective and subjective success rates in the short and long term (Level 1).[1,221,222] It is suitable for patients with urethral hypermobility, and the success rate is low in patients with urethral sphincter deficiency (Level 4).

d. Laparoscopic retropubic colposuspension: Recommendation Grade B
The objective and subjective success rates are good in the short term (Level 2). However, it has been reported that the mid- and long-term outcomes are somewhat inferior, compared to open abdominal retropubic colposuspension and TVT surgery.[1,223,224]

e. Anterior colporrhaphy: Recommendation Grade D
The mid- to long-term outcomes are poor, and repeated surgery might be needed. This procedure should not be performed for stress urinary incontinence.[1,225]

f. Needle bladder neck suspension: Recommendation Grade D
The mid- to long-term outcomes are poor, and this procedure should not be performed for stress urinary incontinence.[1,226]

g. Periurethral injection of bulking agent: Recommendation grade to be determined (off-label)
While effective for the short term, over time, recurrence is common (Level 2).[1] At present, there are no preparations for injections that can be used in Japan. According to the Cochrane Database of Systematic Reviews, there are eight articles pertaining to comparative studies of preparations for injection. According to these studies, although urinary incontinence was improved with silicon particles (Macroplastique®), calcium hydroxyapatite (Coaptite®), ethylene/vinyl alcohol (Tegress®), carbon-coated zirconium beads (Durasphere®) and dextranome/hyaluronic acid copolymer (Zuidex®), the effects were the greatest with GAX collagen (Contigen®).[1,227] Zuidex® and Contigen® have already been withdrawn from the market.

h. Artificial urinary sphincter: Recommendation Grade C1
Artificial urinary sphincter is indicated for limited cases such as patients in whom urinary incontinence surgery is ineffective and patients with severe urinary sphincter deficiency such as in spina bifida (Level 3).[1,228–230] In Japan, the AMS800® urinary control system became covered by health insurance in 2012 (disease name for insurance coverage: urinary incontinence caused by intrinsic urethral sphincter deficiency).

2. Bladder dilatation (augmentation) for OAB and low-compliance bladder: Recommendation Grade C1
Bladder dilatation is indicated for patients with upper urinary tract disorder who do not respond to other treatments and when considerable impairment to social life occurs as a result of urinary incontinence (Level 5).[1,231] There is insufficient evidence supporting the long-term effectiveness of autogenous bladder dilatation (auto-augmentation or detrusor myectomy).[1]

Other treatment methods

1. Indwelling urinary catheterization: Recommendation Grade C1
   Long-term indwelling catheterization carries a high incidence of complications and loss of QOL.[1] Indwelling catheterization is indicated only when other treatments cannot be performed (Level 5).
2. Clean intermittent (self-)catheterization: Recommendation Grade B
   Clean intermittent catheterization is superior to indwelling catheterization for improving patient QOL and results in significantly fewer symptomatic urinary tract infections (Level 2).[1,232]

Conflict of interest

Satoru Takahashi has received research grants from Astellas, Kissei, Nippon Shinyaku, Daiichi Sankyo, Taiho and Takeda, and lecture fees from Astellas, Pfizer, Kissei, Kyorin, Taiho, GlaxoSmithKline and Ferring. Mineo Takei has received consultancy fees from Boston Scientific and Taiho, and lecture fees from Astellas, Kissei, Pfizer and Boston Scientific. Hirotaka Asakura has received research grants from Astellas. Momokazu Gotoh has received research grants from Astellas, Asahi Kasei, Daiichi Sankyo, Nippon Shinyaku, GlaxoSmithKline and Taiho, and lecture fees from Astellas, Daiichi Sankyo, Taiho, Nippon Shinyaku, GlaxoSmithKline, Pfizer and Kyorin. Osamu Ishizuka has received research grants from Astellas, Ono and Takeda, and lecture fees from Astellas and Kissei. Kumiko Kato has received consultancy fees from Unicharm and Taiho, and lecture fees from Astellas, Kissei and Pfizer. Masayasu Koyama and Masami Takeyama have no conflict of interest. Hikaru Tomoe has received lecture fees from Astellas and Kyorin. Tomonori Yamanishi has received research grants from Astellas, Taiho, Kyorin, Nippon Shinyaku and Daiichi Sankyo, and lecture fees from Kissei, GlaxoSmithkline, Astellas and Pfizer. Osamu Yokoyama has received consultancy fees from Kyorin, Astellas and GlaxoSmithkline, research grants from Astellas and Nippon Shinyaku, and lecture fees from Astellas, Pfizer, Kissei and Nippon Shinyaku. Masaki Yoshida has received consultancy fees from Kyorin and Astellas, grants from Astellas, and lecture fees from Kyorin, Astellas, Kissei, Pfizer, Taiho and Ferring. Yasukuni Yoshimura has no conflict of interest. Tsuyoshi Yoshizawa has received lecture fees from Taiho.

References

1 Takahashi S, Takei M, Nishizawa O *et al*. Clinical guideline for female lower urinary tract symptoms. *Low. Urin. Tract Symptoms* 2016; **8**: 5–29.
2 The Japanese Continence Society, ed. Clinical Guidelines for Overactive Bladder, 2nd edn. Richhill: RichHill Medical; 2015.
3 Committee for Establishment of the Clinical Guidelines for Nocturia of the Neurogenic Bladder Society. Clinical guidelines for nocturia. *Int. J. Urol.* 2010; **17**: 397–409.
4 Kobashi KC, Albo ME, Dmochowski RR *et al*. Surgical treatment of female stress urinary incontinence: AUA/SUFU Guideline. *J. Urol.* 2017; **198**: 875.
5 Burkhard FC, Bosch JLHR, Cruz F *et al*. EAU Guidelines on Urinary Incontinence in Adults. 2018. [Cited 27 Jun 2019.] Available from URL: https://uroweb.org/wp-content/uploads/EAU-Guidelines-on-Urinary-Incontinence_2018-V3.pdf.
6 Abrams P, Cardozo L, Wagg A, Wein A (eds). *Incontinence*. 6th edn. Bristol: International Continence Society, 2017.
7 Slieker-ten Hove MCP, Pool-Goudzwaard AL, Eijkemans MJC *et al*. The prevalence of pelvic organ prolapse symptoms and signs and their relation with bladder and bowel disorders in a general female population. *Int. Urogynecol. J. Pelvic Floor Dysfunct.* 2009; **20**: 1037–45.
8 Lawrence JM, Lukacz ES, Nager CW *et al*. Prevalence and co-occurrence of pelvic floor disorders in community-dwelling women. *Obstet. Gynecol.* 2008; **111**: 678–85.
9 Obinata D, Yamaguchi K, Ito A *et al*. Lower urinary tract symptoms in female patients with pelvic organ prolapse: efficacy of pelvic floor reconstruction. *Int. J. Urol.* 2014; **21**: 301–7.
10 FitzGerald MP, Kulkami N, Fenner D. Postoperative resolution of urinary retention in patients with advanced pelvic organ prolapse. *Am. J. Obstet. Gynecol.* 2000; **183**: 1361–3.
11 Frigerio M, Manodoro S, Cola A *et al*. Detrusor underactivity in pelvic organ prolapse. *Int. Urogynecol. J.* 2018; **29**: 1111–6.
12 Rosen RC, Link CL, O'Leary MP *et al*. Lower urinary tract symptoms and sexual health: the role of gender, lifestyle and medical comorbidities. *BJU Int.* 2009; **103**(Suppl 3): 42–7.
13 Hansen BL. Lower urinary tract symptoms (LUTS) and sexual function in both sexes. *Eur. Urol.* 2004; **46**: 229–34.
14 Apostolidis A, Rantell A, Anding R *et al*. How does lower urinary tract dysfunction (LUTD) affect sexual function in men and women? ICI-RS 2015-Part 2. *Neurourol. Urodyn.* 2017; **36**: 869–75.
15 Sako T, Inoue M, Watanabe T *et al*. Impact of overactive bladder and lower urinary tract symptoms on sexual health in Japanese women. *Int. Urogynecol. J.* 2011; **22**: 165–9.
16 Rogers R, Bachmann G, Jumadilova Z *et al*. Efficacy of tolterodine on overactive bladder symptoms and sexual and emotional quality of life in sexually active women. *Int. Urogynecol. J. Pelvic Floor Dysfunct.* 2008; **19**: 1551–7.
17 Zachariou A, Filiponi M. The effect of extended release tolterodine used for overactive bladder treatment on female sexual function. *Int. Braz. J. Urol.* 2017; **43**: 713–20.
18 Zachariou A, Mamoulakis C, Filiponi M *et al*. The effect of mirabegron, used for overactive bladder treatment, on female sexual function: a prospective controlled study. *BMC Urol.* 2018; **18**: 61.
19 Balzarro M, Rubilotta E, Braga A *et al*. OnabotulinumtoxinA detrusor injection improves female sexual function in women with overactive bladder wet syndrome. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 2018; **225**: 228–31.
20 Lau HH, Huang WC, Su TH. Urinary leakage during sexual intercourse among women with incontinence: incidence and risk factors. *PLoS One* 2017; **12**: e0177075.
21 Doğan K, Vural M, Akyüz F. Evaluation of effects of urinary incontinence subtypes on women's sexual function using the Golombok-Rust Inventory of Sexual Satisfaction. *J. Obstet. Gynaecol. Res.* 2017; **43**: 551–6.
22 Grzybowska ME, Wydra DG. Coital incontinence: a factor for deteriorated health-related quality of life and sexual function in women with urodynamic stress urinary incontinence. *Int. Urogynecol. J.* 2017; **28**: 697–704.
23 El-Azab AS, Yousef HA, Seifeldein GS. Coital incontinence: relation to detrusor overactivity and stress incontinence. *Neurourol. Urodyn.* 2011; **30**: 520–4.
24 Aslan E, Gungor Ugurlucan F, Bilgic D *et al*. Effects of transobturator midurethral sling surgery on sexual functions: one-year follow-up. *Gynecol. Obstet. Invest.* 2018; **83**: 187–97.
25 Mengerink BB, Van Leijsen SAL, Vierhout ME *et al*. The impact of midurethral sling surgery on sexual activity and function in women with stress urinary incontinence. *J. Sex. Med.* 2016; **13**: 1498–507.
26 Lindquist AS, Glavind K. Long-term follow-up of sexual function in women before and after tension-free vaginal tape operation for stress urinary incontinence. *Int. Urogynecol. J.* 2016; **27**: 1571–6.
27 Mazouni C, Karsenty G, Bretelle F *et al*. Urinary complications and sexual function after the tension-free vaginal tape procedure. *Acta Obstet. Gynecol. Scand.* 2004; **83**: 955–61.
28 Kinjo M, Yoshimura Y, Kitagawa Y *et al*. Sexual activity and quality of life in Japanese pelvic organ prolapse patients after transvaginal mesh surgery. *J. Obstet. Gynaecol. Res.* 2018; **44**: 1302–7.

29 Lucot J-P, Cosson M, Bader G *et al*. Safety of vaginal mesh surgery versus laparoscopic mesh sacropexy for cystocele repair: results of the prosthetic pelvic floor repair randomized controlled trial. *Eur. Urol.* 2018; **74**: 167–76.

30 Takahashi S, Obinata D, Sakuma T *et al*. Tension-free vaginal mesh procedure for pelvic organ prolapse: a single-center experience of 310 cases with 1-year follow up. *Int. J. Urol.* 2010; **17**: 353–8.

31 Cody JD, Jacobs ML, Richardson K, Moehrer B, Hextall A. Oestrogen therapy for urinary incontinence in post-menopausal women. *Cochrane Database Syst. Rev.* 2012; (10): CD001405.

32 Weber MA, Kleijn MH, Langendam M *et al*. Local oestrogen for pelvic floor disorders: a systematic review. *PLoS One* 2015; **10**: e0136265.

33 Tseng L-H, Wang AC, Chang Y-L *et al*. Randomized comparison of tolterodine with vaginal estrogen cream versus tolterodine alone for the treatment of postmenopausal women with overactive bladder syndrome. *Neurourol. Urodyn.* 2009; **28**: 47–51.

34 Serati M, Salvatore S, Uccella S *et al*. Is there a synergistic effect of topical oestrogens when administered with antimuscarinics in the treatment of symptomatic detrusor overactivity? *Eur. Urol.* 2009; **55**: 713–9.

35 Maman K, Aballea S, Nazir J *et al*. Comparative efficacy and safety of medical treatments for the management of overactive bladder: a systematic literature review and mixed treatment comparison. *Eur. Urol.* 2014; **65**: 755–65.

36 Kelleher C, Hakimi Z, Zur R *et al*. Efficacy and tolerability of mirabegron compared with antimuscarinic monotherapy or combination therapies for overactive bladder: a systematic review and network meta-analysis. *Eur. Urol.* 2018; **74**: 324–33.

37 Madhuvrata P, Cody JD, Ellis G *et al*. Which anticholinergic drug for overactive bladder symptoms in adults. *Cochrane Database Syst. Rev.* 2012; (1): CD005429.

38 Nazir J, Kelleher C, Aballéa S *et al*. Comparative efficacy and tolerability of solifenacin 5 mg/day versus other oral antimuscarinic agents in overactive bladder: a systematic literature review and network meta-analysis. *Neurourol Urodyn* 2018; **37**: 986–96.

39 Abrams P, Kelleher C, Staskin D *et al*. Combination treatment with mirabegron and solifenacin in patients with overactive bladder: efficacy and safety results from a randomised, double-blind, dose-ranging, phase 2 study (Symphony). *Eur. Urol.* 2015; **67**: 577–88.

40 Drake MJ, Chapple C, Esen AA *et al*.; BESIDE study investigators. Efficacy and safety of mirabegron add-on therapy to solifenacin in incontinent overactive bladder patients with an inadequate response to initial 4-week solifenacin monotherapy: a randomised double-blind multicentre phase 3B study (BESIDE). *Eur. Urol.* 2016; **70**: 136–45.

41 Herschorn S, Chapple CR, Abrams P *et al*. Efficacy and safety of combinations of mirabegron and solifenacin compared with monotherapy and placebo in patients with overactive bladder (SYNERGY study). *BJU Int.* 2017; **120**: 562–75.

42 Yamaguchi O, Kakizaki H, Homma Y *et al*. Safety and efficacy of mirabegron as 'add-on' therapy in patients with overactive bladder treated with solifenacin: a post-marketing, open-label study in Japan (MILAI study). *BJU Int.* 2015; **116**: 612–22.

43 Gratzke C, van Maanen R, Chapple C *et al*. Long-term safety and efficacy of mirabegron and solifenacin in combination compared with monotherapy in patients with overactive bladder: a randomised, multicentre phase 3 study (SYNERGY II). *Eur. Urol.* 2018; **74**: 501–9.

44 Yamaguchi O, Kakizaki H, Homma Y *et al*. Long-term safety and efficacy of antimuscarinic add-on therapy in patients with overactive bladder who had a suboptimal response to mirabegron monotherapy: a multicenter, randomized study in Japan (MILAI II study). *Int. J. Urol.* 2019; **26**: 342–52.

45 Yoshida M, Kakizaki H, Takahashi S *et al*. Long-term safety and efficacy of the novel β3-adrenoreceptor agonist vibegron in Japanese patients with overactive bladder: a phase III prospective study. *Int. J. Urol.* 2018; **25**: 668–75.

46 Mitcheson HD, Samanta S, Muldowney K *et al*. Vibegron (RVT-901/MK-4618/KRP-114V) administered once daily as monotherapy or concomitantly with tolterodine in patients with an overactive bladder: a multicenter, phase IIb, randomized, double-blind, controlled trial. *Eur. Urol.* 2019; **75**: 274–82.

47 Yoshida M, Kato D, Nishimura T *et al*. Anticholinergic burden in the Japanese elderly population: Use of antimuscarinic medications for overactive bladder patients. *Int. J. Urol.* 2018; **25**: 855–62.

48 Fox C, Richardson K, Maidment ID *et al*. Anticholinergic medication use and cognitive impairment in the older population: the Medical Research Council Cognitive Function and Ageing Study. *J. Am. Geriatr. Soc.* 2011; **59**: 1477–83.

49 Chen SF, Kuo HC. Therapeutic efficacy of low-dose (25 mg) mirabegron therapy for patients with mild to moderate overactive bladder symptoms due to central nervous system diseases. *Low. Urin. Tract Symptoms* 2019; **11**: O53–O58.

50 Nozawa Y, Kato D, Tabuchi H, Kuroishi K. Safety and effectiveness of mirabegron in patients with overactive bladder in a real-world clinical setting: a Japanese post-marketing study. *Low. Urin. Tract Symptoms* 2018; **10**: 122–30.

51 Goldfischer ER, Sand PK, Thomas H, Peters-Gee J. Efficacy and safety of oxybutynin topical gel 3% in patients with urgency and/or mixed urinary incontinence: a randomized, double-blind, placebo-controlled study. *Neurourol. Urodyn.* 2015; **34**: 37–43.

52 Staskin DR, Te AE. Short- and long-term efficacy of solifenacin treatment in patients with symptoms of mixed urinary incontinence. *BJU Int.* 2006; **97**: 1256–61.

53 Kelleher C, Cardozo L, Kobashi K, Lucente V. Solifenacin: as effective in mixed urinary incontinence as in urgency urinary incontinence. *Int. Urogynecol. J. Pelvic Floor Dysfunct.* 2006; **17**: 382–8.

54 Dmochowski RR, Nitti V, Staskin D *et al*. Transdermal oxybutynin in the treatment of adults with overactive bladder: combined results of two randomized clinical trials. *World J. Urol.* 2005; **23**: 263–70.

55 Khullar V, Hill S, Laval KU *et al*. Treatment of urgency-predominant mixed urinary incontinence with tolterodine extended release: a randomized, placebo-controlled trial. *Urology* 2004; **64**: 269–74.

56 Lee EW, Kobashi KC. Mixed incontinence: what takes precedence in its management? *Curr. Urol. Rep.* 2014; **15**: 461.

57 Abdel-Fattah M, Hopper LR, Mostafa A. Evaluation of transobturator tension-free vaginal tapes in the surgical management of mixed urinary incontinence: 3-year outcomes of a randomized controlled trial. *J. Urol.* 2014; **191**: 114–9.

58 Paick JS, Oh SJ, Kim SW, Ku JH. Tension-free vaginal tape, suprapubic arc sling, and transobturator tape in the treatment of mixed urinary incontinence in women. *Int. Urogynecol. J. Pelvic Floor Dysfunct.* 2008; **19**: 123–9.

59 Lee JK, Dwyer PL, Rosamilia A *et al*. Persistence of urgency and urgency urinary incontinence in women with mixed urinary symptoms after midurethral slings: a multivariate analysis. *BJOG* 2011; **118**: 798–805.

60 Natale F, Illiano E, La Penna C *et al*. Mixed urinary incontinence: a prospective study on the effect of transobturator mid-urethral sling. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 2018s; **221**: 64–9.

61 Kulseng-Hanssen S, Husby H, Schiotz HA. The tension free vaginal tape operation for women with mixed incontinence: do preoperative variables predict the outcome? *Neurourol. Urodyn.* 2007; **26**: 115–21.

62 Al-Mandeel H, Ross S, Robert M, Milne J. Incidence of stress urinary incontinence following vaginal repair of pelvic organ prolapse in objectively continent women. *Neurourol. Urodyn.* 2011; **30**: 390–4.

63 Christmann-Schmid C, Bruehlmann E, Koerting I, Krebs J. Laparoscopic sacrocolpopexy with or without midurethral sling insertion: is a two-step approach justified? A prospective study. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 2018; **229**: 98–102.

64 Wei JT, Nygaard I, Richter HE *et al*. Pelvic Floor Disorders Network. A midurethral sling to reduce incontinence after vaginal prolapse repair. *N. Engl. J. Med.* 2012; **366**: 2358–67.

65 van der Ploeg JM, Oude Rengerink K, van der Steen A *et al*. Dutch Urogynaecology Consortium. Transvaginal prolapse repair with or without the addition of a midurethral sling in women with genital prolapse and stress urinary incontinence: a randomised trial. *BJOG*. 2015; **122**: 1022–30.

66 Groutz A, Gold R, Pauzner D *et al*. Tension-free vaginal tape (TVT) for the treatment of occult stress urinary incontinence in women undergoing prolapse repair: a prospective study of 100 consecutive cases. *Neurourol. Urodyn.* 2004; **23**: 632–5.

67 Trabuco EC, Klingele CJ, Blandon RE *et al*. Burch retropubic urethropexy compared with midurethral sling with concurrent sacrocolpopexy: a randomized controlled trial. *Obstet. Gynecol.* 2016; **128**: 828–35.

68 Schierlitz L, Dwyer PL, Rosamilia A *et al*. Pelvic organ prolapse surgery with and without tension-free vaginal tape in women with occult or asymptomatic urodynamic stress incontinence: a randomised controlled trial. *Int. Urogynecol. J.* 2014; **25**: 33–40.

69 Baessler K, Christmann-Schmid C, Maher C *et al*. Surgery for women with pelvic organ prolapse with or without stress urinary incontinence. *Cochrane Database Syst. Rev.* 2018; (8): CD013108.

70 Abrams P, Cardozo L, Fall M *et al*. The standardisation of terminology of lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. *Neurourol. Urodyn.* 2002; **21**: 167–78.

71 Homma Y, Gotoh M, Kawauchi A *et al*. Clinical guidelines for male lower urinary tract symptoms and benign prostatic hyperplasia. *Int. J. Urol.* 2017; **24**: 716–29.

72 Schatzl G, Temml C, Waldmüller J *et al*. A comparative cross-sectional study of lower urinary tract symptoms in both sexes. *Eur. Urol.* 2001; **40**: 213–9.

73 Homma Y, Yamaguchi O, Hayashi K.; Neurogenic Bladder Society Committee. Epidemiologic survey of lower urinary tract symptoms in Japan. *Urology* 2006; **68**: 560–4.

74 Lepor H, Machi G. Comparison of AUA symptom index in unselected males and females between fifty-five and seventy-nine years of age. *Urology* 1993; **42**: 36–41.

75 Portman DJ, Gass MLVulvovaginal Atrophy Terminology Consensus Conference Panel. Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and the North American Menopause Society. *Menopause* 2014; **21**: 1063–8.

76 Irwin DE, Milsom I, Hunskaar S *et al*. Population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in five countries: results of the EPIC study. *Eur. Urol.* 2006; **50**: 1306–15.

77 Coyne KS, Sexton CC, Thompson CL *et al*. The prevalence of lower urinary tract symptoms (LUTS) in the USA, the UK and Sweden: results from the Epidemiology of LUTS (EpiLUTS) study. *BJU Int.* 2009; **104**: 352–60.

78 Wang Y, Hu H, Xu K *et al*. Prevalence, risk factors and the bother of lower urinary tract symptoms in China: a population-based survey. *Int. Urogynecol. J.* 2015; **26**: 911–9.

79 Homma Y, Yamaguchi O, Hayashi K the Members of the Neurogenic Bladder Society Committee. An epidemiological survey of overactive bladder symptoms in Japan. *BJU Int.* 2005; **96**: 1314–8.

80 Cerruto MA, D'Elia C, Aloisi A *et al*. Prevalence, incidence and obstetric factors' impact on female urinary incontinence in Europe: a systematic review. *Urol. Int.* 2013; **90**: 1–9.

81 Reigota RB, Pedro AO, de Souza Santos Machado V *et al*. Prevalence of urinary incontinence and its association with multimorbidity in women aged 50 years or older: a population-based study. *Neurourol. Urodyn.* 2016; **35**: 62–8.

82 MacArthur C, Wilson D, Herbison P *et al*. Prolong study group. Urinary incontinence persisting after childbirth: extent, delivery history, and effects in a 12-year longitudinal cohort study. *BJOG* 2016; **123**: 1022–9.

83 Juliato CRT, Baccaro LF, Pedro AO *et al*. Factors associated with urinary incontinence in middle-aged women: a population-based household survey. *Int. Urogynecol. J.* 2017; **28**: 423–9.

84 Ng K, Cheung RYK, Lee LL *et al*. An observational follow-up study on pelvic floor disorders to 3–5 years after delivery. *Int. Urogynecol. J.* 2017; **28**: 1393–9.

85 Gyhagen M, Bullarbo M, Nielsen TF, Milsom I. Prevalence and risk factors for pelvic organ prolapse 20 years after childbirth: a national cohort study in singleton primiparae after vaginal or caesarean delivery. *BJOG* 2013; **120**: 152–60.

86 Wu JM, Vaughan CP, Goode PS *et al*. Prevalence and trends of symptomatic pelvic floor disorders in U.S. women. *Obstet Gynecol* 2014; **123**: 141–8.

87 Homma Y, Yoshida M, Yamanishi T, Gotoh M. Core Lower Urinary Tract Symptom Score (CLSS) questionnaire: a reliable tool in the overall assessment of lower urinary tract symptoms. *Int. J. Urol.* 2008; **15**: 816–20.

88 Fujimura T, Kume H, Tsurumaki Y *et al*. Core lower urinary tract symptom score (CLSS) for the assessment of female lower urinary tract symptoms: a comparative study. *Int. J. Urol.* 2011; **18**: 778–84.

89 Fujimura T, Kume H, Nishimatsu H *et al*. Assessment of lower urinary tract symptoms in men by international prostate symptom score and core lower urinary tract symptom score. *BJU Int.* 2012; **109**: 1512–6.

90 Coyne K, Revicki D, Hunt T *et al*. Psychometric validation of an overactive bladder symptom and health-related quality of life questionnaire: the OAB-q. *Qual. Life Res.* 2002; **11**: 563–74.

91 Abraham L, Hareendran A, Mills IW *et al*. Development and validation of a quality-of-life measure for men with nocturia. *Urology* 2004; **63**: 481–6.

92 Homma Y, Kakizaki H, Yamaguchi O *et al*. Assessment of overactive bladder symptoms: comparison of 3-day bladder diary and the overactive bladder symptoms score. *Urology* 2011; **77**: 60–4.

93 Koch M, Rauchenwald T, Kivaranovic D *et al*. Association of uterine leiomyoma and overactive bladder syndrome. *Int. J. Gynaecol. Obstet.* 2018; **142**: 365–9.

94 de Resende Júnior JAD, Crispi CP, Cardeman L *et al*. Urodynamic observations and lower urinary tract symptoms associated with endometriosis: a prospective cross-sectional observational study assessing women with deep infiltrating disease. *Int. Urogynecol. J.* 2018; **29**: 1349–58.

95 Hristov KL, Parajuli SP, Provence A *et al*. Nongenomic modulation of the large conductance voltage- and Ca^{2+}-activated K^{+} channels by estrogen: a novel regulatory mechanism in human detrusor smooth muscle. *Physiol. Rep.* 2017; **5**: e13351.

96 Matsuo T, Miyata Y, Sakai H. Daily salt intake is an independent risk factor for pollakiuria and nocturia. *Int. J. Urol.* 2017; **24**: 384–9.

97 Yokoyama O, Nishizawa O, Homma Y*et al*. OASIS Project Group. Nocturnal polyuria and hypertension in patients with lifestyle related diseases and overactive bladder. *J. Urol.* 2017; **197**: 423–31.

98 Smith AL, Hantsoo L, Malykhina AP *et al*. Basal and stress-activated hypothalamic pituitary adrenal axis function in postmenopausal women with overactive bladder. *Int. Urogynecol. J.* 2016; **27**: 1383–91.

99 Davenport MT, Sokol ER, Comiter CV, Elliott CS. Does the degree of cystocele predict de novo stress urinary incontinence after prolapse repair? Further analysis of the Colpopexy and Urinary Reduction Efforts Trial. *Female Pelvic Med. Reconstr. Surg.* 2018; **24**: 292–4.

100 Tomoe H. Improvement of overactive bladder symptoms after tension-free vaginal mesh operation in women with pelvic organ prolapse: correlation with preoperative urodynamic findings. *Int. J. Urol.* 2015; **22**: 577–80.

101 Abdullah B, Nomura J, Moriyama S *et al*. Clinical and urodynamic assessment in patients with pelvic organ prolapse before and after laparoscopic sacrocolpopexy. *Int. Urogynecol. J.* 2017; **28**: 1543–9.

102 Zacharakis D, Grigoriadis T, Pitsouni E *et al*. Assessment of overactive bladder symptoms among women with successful pessary placement. *Int. Urogynecol. J.* 2018; **29**: 571–7.

103 Osman NI, Chapple CR, Abrams P *et al*. Detrusor underactivity and the underactive bladder: a new clinical entity? A review of current terminology, definitions, epidemiology, aetiology, and diagnosis. *Eur. Urol.* 2014; **65**: 389–98.

104 Aldamanhori R, Inman R. The treatment of complex female urethral pathology. *Asian J. Urol.* 2018; **5**: 160–3.

105 Homma Y, Ando T, Yoshida M *et al*. Voiding and incontinence frequencies: variability of diary data and required diary length. *Neurourol. Urodyn.* 2002; **21**: 204–9.

106 Ku JH, Jeong IG, Lim DJ *et al*. Voiding diary for the evaluation of urinary incontinence and lower urinary tract symptoms: prospective assessment of patient compliance and burden. *Neurourol. Urodyn.* 2004; **23**: 331–5.

107 Homma Y, Yamaguchi O, Kageyama S *et al*. Nocturia in the adult: classification on the basis of largest voided volume and nocturnal urine production. *J. Urol.* 2000; **163**: 777–81.

108 Krhut J, Zachoval R, Smith PP *et al*. Pad weight testing in the evaluation of urinary incontinence. *Neurourol. Urodyn.* 2014; **33**: 507–10.

109 Plotti F, Angioli R, Zullo MA *et al*. Update on urodynamic bladder dysfunctions after radical hysterectomy for cervical cancer. *Crit. Rev. Oncol. Hematol.* 2011; **80**: 323–9.

110 Clemons JL, LaSala CA. The tension-free vaginal tape in women with a non-hypermobile urethra and low maximum urethral closure pressure. *Int. Urogynecol. J. Pelvic Floor Dysfunct.* 2007; **18**: 727–32.

111 Harris N, Swithinbank L, Hayek SA *et al*. Can maximum urethral closure pressure (MUCP) be used to predict outcome of surgical treatment of stress urinary incontinence? *Neurourol. Urodyn.* 2011; **30**: 1609–12.

112 Burden H, Warren K, Abrams P. Leak point pressures: how useful are they? *Curr. Opin. Urol.* 2015; **25**: 317–22.

113 Pajoncini C, Costantini E, Guercini F *et al*. Clinical and urodynamic features of intrinsic sphincter deficiency. *Neurourol. Urodyn.* 2003; **22**: 264–8.

114 Solomon E, Yasmin H, Jenks J *et al*. The development and validation of a new nomogram for diagnosing bladder outlet obstruction in women. *J. Urol.* 2014; **191**(4 Suppl): e882.

115 Dybowski B, Bres-Niewada E, Radziszewski P. Pressure-flow nomogram for women with lower urinary tract symptoms. *Arch. Med. Sci.* 2014; **10**: 752–6.

116 Gammie A, Kirschner-Hermanns R, Rademakers K. Evaluation of obstructed voiding in the female: how close are we to a definition? *Curr. Opin. Urol.* 2015; **25**: 292–5.

117 Meier K, Padmanabhan P. Female bladder outlet obstruction: an update on diagnosis and management. *Curr. Opin. Urol.* 2016; **26**: 334–41.

118 Homma Y, Akiyama Y, Tomoe H *et al*. Clinical guidelines for interstitial cystitis/painful bladder syndrome. *Int. J. Urol.* 2020; **27**: 578–89.

119 Raman SP, Fishman EK. Upper and lower tract urothelial imaging using computed tomography urography. *Urol. Clin. North Am.* 2018; **45**: 389–405.

120 Lienemann A, Sprenger D, Janßen U *et al*. Assessment of pelvic organ descent by use of functional cine-MRI: which reference line should be used? *Neurourol. Urodyn.* 2004; **23**: 33–7.

121 Gozukara YM, Akalan G, Tok EC *et al*. The improvement in pelvic floor symptoms with weight loss in obese women does not correlate with the changes in pelvic anatomy. *Int. Urogynecol. J.* 2014; **25**: 1219–25.

122 Imamura M, Williams K, Wells M, McGrother C Lifestyle interventions for the treatment of urinary incontinence in adults. *Cochrane Database Syst Rev* 2015; (12): CD003505.

123 Breyer BN, Creasman JM, Richter HE *et al*. PRIDE. A behavioral weight loss program and nonurinary incontinence lower urinary tract symptoms in overweight and obese women with urinary incontinence: a secondary data analysis of PRIDE. *J. Urol.* 2018; **199**: 215–22.

124 Breyer BN, Phelan S, Hogan PE*et al*. Look AHEAD Research Group. Intensive lifestyle intervention reduces urinary incontinence in overweight/obese men with type 2 diabetes: results from the Look AHEAD trial. *J. Urol.* 2014; **192**: 144–9.

125 Phelan S, Kanaya AM, Ma Y*et al*.; Diabetes Prevention Program Research Group. Long-term prevalence and predictors of urinary incontinence among women in the Diabetes Prevention Program Outcomes Study. *Int. J. Urol.* 2015; **22**: 206–12.

126 Maserejian NN, Kupelian V, Miyasato G *et al*. Are physical activity, smoking and alcohol consumption associated with lower urinary tract symptoms in men or women? Results from a population based observational study. *J. Urol.* 2012; **188**: 490–5.

127 Kim H, Yoshida H, Suzuki T. The effects of multidimensional exercise on functional decline, urinary incontinence, and fear of falling in community-dwelling elderly women with multiple symptoms of geriatric syndrome: a randomized controlled and 6-month follow-up trial. *Arch. Gerontol. Geriatr.* 2011; **52**: 99–105.

128 Talley KMC, Wyman JF, Bronas U *et al*. Defeating urinary incontinence with exercise training: results of a pilot study in frail older women. *J. Am. Geriatr. Soc.* 2017; **65**: 1321–7.

129 Vinsnes AG, Helbostad JL, Nyrønning S*et al*. Effect of physical training on urinary incontinence: a randomized parallel group trial in nursing homes. *Clin. Interv. Aging* 2012; **7**: 45–50.

130 Huang AJ, Jenny HE, Chesney MA *et al*. A group-based yoga therapy intervention for urinary incontinence in women: a pilot randomized trial. *Female Pelvic Med. Reconstr. Surg.* 2014; **20**: 147–54.

131 Madhu CK, Hashim H, Enki D, Drake MJ. Risk factors and functional abnormalities associated with adult onset secondary nocturnal enuresis in women. *Neurourol. Urodyn.* 2017; **36**: 188–91.

132 Madhu C, Enki D, Drake MJ, Hashim H. The functional effects of cigarette smoking in women on the lower urinary tract. *Urol. Int.* 2015; **95**: 478–82.

133 Robinson D, Hanna-Mitchell A, Rantell A *et al*. Are we justified in suggesting change to caffeine, alcohol, and carbonated drink intake in lower urinary tract disease? Report from the ICI-RS 2015. *Neurourol. Urodyn.* 2017; **36**: 876–81.

134 Gleason JL, Richter HE, Redden DT *et al*. Caffeine and urinary incontinence in US women. *Int. Urogynecol. J.* 2013; **24**: 295–302.

135 Hirayama F, Lee AH. Is caffeine intake associated with urinary incontinence in Japanese adults? *J. Prev. Med. Public Health* 2012; **45**: 204–8.

136 Baek JM, Song JY, Lee SJ *et al*. Caffeine intake is associated with urinary incontinence in Korean postmenopausal women: results from the Korean National Health and Nutrition Examination survey. *PLoS One* 2016; **11**: e0149311.

137 Wells MJ, Jamieson K, Markham TCW *et al*. The effect of caffeinated versus decaffeinated drinks on overactive bladder: a double-blind, randomized, crossover study. *J. Wound Ostomy Continence Nurs.* 2014; **41**: 371–8.

138 Maserejian NN, Wager CG, Giovannucci EL *et al*. Intake of caffeinated, carbonated, or citrus beverage types and development of lower urinary tract symptoms in men and women. *Am. J. Epidemiol.* 2013; **177**: 1399–410.

139 Townsend MK, Resnick NM, Grodstein F. Caffeine intake and risk of urinary incontinence progression among women. *Obstet. Gynecol.* 2012; **119**: 950–7.

140 Townsend MK, Devore EE, Resnick NM, Grodstein F. Acidic fruit intake in relation to incidence and progression of urinary incontinence. *Int. Urogynecol. J.* 2013; **24**: 605–12.

141 Lee AH, Hirayama F. Alcohol consumption and female urinary incontinence: a community-based study in Japan. *Int. J. Urol.* 2012; **19**: 143–8.

142 Wood LN, Markowitz MA, Parameshwar PS *et al*. Is it safe to reduce water intake in the overactive bladder population? A systematic review. *J. Urol.* 2018; **200**: 375–81.

143 Dumoulin C, Hay-Smith J, Frawley H *et al*.; International Continence Society. 2014 consensus statement on improving pelvic floor muscle training adherence: International Continence Society 2011 State-of-the-Science Seminar. *Neurourol. Urodyn.* 2015; **34**: 600–5.

144 Dumoulin C, Cacciari LP, Hay-Smith EJC. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women. *Cochrane Database Syst. Rev.* 2018; (10): CD005654.

145 Celiker Tosun O, Kaya Mutlu E, Ergenoglu AM *et al*. Does pelvic floor muscle training abolish symptoms of urinary incontinence? A randomized controlled trial. *Clin. Rehabil.* 2015; **29**: 525–37.

146 Labrie J, Berghmans BLCM, Fischer K *et al*. Surgery versus physiotherapy for stress urinary incontinence. *N. Engl. J. Med.* 2013; **369**: 1124–33.

147 McLean L, Varette K, Gentilcore-Saulnier E *et al*. Pelvic floor muscle training in women with stress urinary incontinence causes hypertrophy of the urethral sphincters and reduces bladder neck mobility during coughing. *Neurourol. Urodyn.* 2013; **32**: 1096–102.

148 Borello-France D, Burgio KL, Goode PS *et al*.; Pelvic Floor Disorders Network. Adherence to behavioral interventions for stress incontinence: rates, barriers, and predictors. *Phys. Ther.* 2013; **93**: 757–73.

149 Kafri R, Deutscher D, Shames J *et al*. Randomized trial of a comparison of rehabilitation or drug therapy for urgency urinary incontinence: 1-year follow-up. *Int. Urogynecol. J.* 2013; **24**: 1181–9.

150 Azuri J, Kafri R, Ziv-Baran T, Stav K. Outcomes of different protocols of pelvic floor physical therapy and anti-cholinergics in women with wet overactive bladder: a 4-year follow-up. *Neurourol. Urodyn.* 2017; **36**: 755–8.

151 Rizvi RM, Chughtai NG, Kapadia N. Effects of bladder training and pelvic floor muscle training in female patients with overactive bladder syndrome: a randomized controlled trial. *Urol. Int.* 2018; **100**: 420–7.

152 Boyle R, Hay-Smith EJ, Cody JD, Mørkved S. Pelvic floor muscle training for prevention and treatment of urinary and fecal incontinence in antenatal and postnatal women: a short version Cochrane review. *Neurourol. Urodyn.* 2014; **33**: 269–76.

153 Ko P-C, Liang C-C, Chang S-D *et al*. A randomized controlled trial of antenatal pelvic floor exercises to prevent and treat urinary incontinence. *Int. Urogynecol. J.* 2011; **22**: 17–22.

154 Stafne SN, Salvesen KÅ, Romundstad PR *et al*. Does regular exercise including pelvic floor muscle training prevent urinary and anal incontinence during pregnancy? A randomised controlled trial. *BJOG* 2012; **119**: 1270–80.

155 Marques J, Botelho S, Pereira LC *et al*. Pelvic floor muscle training program increases muscular contractility during first pregnancy and postpartum: electromyographic study. *Neurourol. Urodyn.* 2013; **32**: 998–1003.

156 Fritel X, de Tayrac R, Bader G *et al*. Preventing urinary incontinence with supervised prenatal pelvic floor exercises: a randomized controlled trial. *Obstet. Gynecol.* 2015; **126**: 370–7.

157 Hilde G, Stær-Jensen J, Siafarikas F *et al*. Postpartum pelvic floor muscle training and urinary incontinence: a randomized controlled trial. *Obstet. Gynecol.* 2013; **122**: 1231–8.

158 Åhlund S, Nordgren B, Wilander E-L *et al*. Is home-based pelvic floor muscle training effective in treatment of urinary incontinence after birth in primiparous women? A randomized controlled trial. *Acta Obstet. Gynecol. Scand.* 2013; **92**: 909–15.

159 Kahyaoglu Sut H, Balkanli KP. Effect of pelvic floor muscle exercise on pelvic floor muscle activity and voiding functions during pregnancy and the postpartum period. *Neurourol. Urodyn.* 2016; **35**: 417–22.

160 Hirakawa T, Suzuki S, Kato K *et al*. Randomized controlled trial of pelvic floor muscle training with or without biofeedback for urinary incontinence. *Int. Urogynecol. J.* 2013; **24**: 1347–54.

161 Ong TA, Khong SY, Ng KL *et al*. Using the vibrance Kegel device with pelvic floor muscle exercise for stress urinary incontinence: a randomized controlled pilot study. *Urology* 2015; **86**: 487–91.

162 Peirce C, Murphy C, Fitzpatrick M *et al*. Randomised controlled trial comparing early home biofeedback physiotherapy with pelvic floor exercises for the treatment of third-degree tears (EBAPT Trial). *BJOG* 2013; **120**: 1240–7.

163 Voorham JC, De Wachter S, Van den Bos TWL *et al*. The effect of EMG biofeedback assisted pelvic floor muscle therapy on symptoms of the overactive bladder syndrome in women: a randomized controlled trial. *Neurourol. Urodyn.* 2017; **36**: 1796–803.

164 Griffiths D, Clarkson B, Tadic SD, Resnick NM. Brain mechanisms underlying urge incontinence and its response to pelvic floor muscle training. *J. Urol.* 2015; **194**: 708–15.

165 Resnick NM, Perera S, Tadic S *et al*. What predicts and what mediates the response of urge urinary incontinence to biofeedback? *Neurourol. Urodyn.* 2013; **32**: 408–15.

166 Rai BP, Cody JD, Alhasso A, Stewart L. Anticholinergic drugs versus non-drug active therapies for non-neurogenic overactive bladder syndrome in adults. *Cochrane Database Syst. Rev.* 2012; (12): CD003193.

167 Lee H-E, Cho SY, Lee S *et al*. Short-term effects of a systematized bladder training program for idiopathic overactive bladder: a prospective study. *Int. Neurourol. J.* 2013; **17**: 11–7.

168 Averbeck MA, Altaweel W, Manu-Marin A, Madersbacher H. Management of LUTS in patients with dementia and associated disorders. *Neurourol. Urodyn.* 2017; **36**: 245–52.

169 Iwatsubo E, Suzuki M, Igawa Y, Homma Y. Individually tailored ultrasound-assisted prompted voiding for institutionalized older adults with urinary incontinence. *Int. J. Urol.* 2014; **21**: 1253–7.

170 Paik S-H, Han S-R, Kwon O-J *et al*. Acupuncture for the treatment of urinary incontinence: a review of randomized controlled trials. *Exp. Ther. Med.* 2013; **6**: 773–80.

171 Engberg S, Cohen S, Sereika SM. The efficacy of acupuncture in treating urge and mixed incontinence in women: a pilot study. *J. Wound Ostomy Continence Nurs.* 2009; **36**: 661–70.

172 Emmons SL, Otto L. Acupuncture for overactive bladder: a randomized controlled trial. *Obstet. Gynecol.* 2005; **106**: 138–43.

173 Kim H, Yoshida H, Suzuki T. Effects of exercise treatment with or without heat and steam generating sheet on urine loss in community-dwelling Japanese elderly women with urinary incontinence. *Geriatr. Gerontol. Int.* 2011; **11**: 452–9.

174 Komesu YM, Sapien RE, Rogers RG, Ketai LH. Hypnotherapy for treatment of overactive bladder: a randomized controlled trial pilot study. *Female Pelvic Med. Reconstr. Surg.* 2011; **17**: 308–13.

175 Todorova A, Vonderheid-Guth B, Dimpfel W. Effects of tolterodine, trospium chloride, and oxybutynin on the central nervous system. *J. Clin. Pharmacol.* 2001; **41**: 636–44.

176 Katz IR, Sands LP, Bilker W *et al*. Identification of medications that cause cognitive impairment in older people: the case of oxybutynin chloride. *J. Am. Geriatr. Soc.* 1998; **46**: 8–13.

177 Ouslander JG, Shih YT, Malone-Lee J, Luber K. Overactive bladder: special considerations in the geriatric population. *Am. J. Manag. Care* 2000; **6** (11 Suppl): S599–S606.

178 Yamaguchi O, Uchida E, Higo N *et al*.; Oxybutynin Patch Study Group. Efficacy and safety of once-daily oxybutynin patch versus placebo and propiverine in Japanese patients with overactive bladder: a randomized double-blind trial. *Int. J. Urol.* 2014; **21**: 586–93.

179 Gotoh M, Yokoyama O, Nishizawa O.; Japanese Propiverine Study Group. Propiverine hydrochloride in Japanese patients with overactive bladder: a randomized, double-blind, placebo-controlled trial. *Int. J. Urol.* 2011; **18**: 365–73.

180 Masumori N, Funato Y, Yamaguchi Y, Itoh K. Evaluation of usefulness of propiverine hydrochloride in poor responders to previous anticholinergics. *Low. Urin. Tract Symptoms* 2018; **10**: 116–21.

181 Minagawa T, Gotoh M, Yokoyama O *et al*.; FRESH study group. Therapeutic effect of propiverine hydrochloride on mixed-type urinary incontinence in women: The Female Urgency and Stress Urinary Incontinence Study of Propiverine Hydrochloride trial. *Int. J. Urol.* 2018; **25**: 486–91.

182 Homma Y, Paick JS, Lee JG, Kawabe K.; Japanese and Korean Tolterodine Study Group. Clinical efficacy and tolerability of extended-release tolterodine and immediate-release oxybutynin in Japanese and Korean patients with an overactive bladder: a randomized, placebo-controlled trial. *BJU Int.* 2003; **92**: 741–7.

183 Wagg A, Dale M, Tretter R *et al*. Randomised, multicentre, placebo-controlled, double-blind crossover study investigating the effect of solifenacin and oxybutynin in elderly people with mild cognitive impairment: the SENIOR study. *Eur. Urol.* 2013; **64**: 74–81.

184 Yamaguchi O, Marui E, Kakizaki H *et al*.; Japanese Solifenacin Study Group. Randomized, double-blind, placebo- and propiverine-controlled trial of the once-daily antimuscarinic agent solifenacin in Japanese patients with overactive bladder. *BJU Int.* 2007; **100**: 579–87.

185 Homma Y, Yamaguchi T, Yamaguchi O.; Imidafenacin Study Group. A randomized, double-blind, placebo controlled phase II dose-finding study of the novel anti-muscarinic agent imidafenacin in Japanese patients with overactive bladder. *Int. J. Urol.* 2008; **15**: 809–15.

186 Homma Y, Yamaguchi O.; Imidafenacin Study Group. A randomized, double-blind, placebo- and propiverine-controlled trial of the novel antimuscarinic agent imidafenacin in Japanese patients with overactive bladder. *Int. J. Urol.* 2009; **16**: 499–506.

187 Chapple C, Schneider T, Haab F *et al*. Superiority of fesoterodine 8 mg vs 4 mg in reducing urgency urinary incontinence episodes in patients with overactive bladder: results of the randomised, double-blind, placebo-controlled EIGHT trial. *BJU Int.* 2014; **114**: 418–26.

188 Wagg A, Khullar V, Marschall-Kehrel D *et al*. Flexible-dose fesoterodine in elderly adults with overactive bladder: results of the randomized, double-blind, placebo-controlled study of fesoterodine in an aging population trial. *J. Am. Geriatr. Soc.* 2013; **61**: 185–93.

189 Dubeau CE, Kraus SR, Griebling TL *et al*. Effect of fesoterodine in vulnerable elderly subjects with urgency urinary incontinence: a double-blind, placebo controlled trial. *J. Urol.* 2014; **191**: 395–404.

190 Oelke M, Becher K, Castro-Diaz D *et al*. Appropriateness of oral drugs for long-term treatment of lower urinary tract symptoms in older persons: results of a systematic literature review and international consensus validation process (LUTS-FORTA 2014). *Age Ageing* 2015; **44**: 745–55.

191 Yamaguchi O, Marui E, Kakizaki H *et al*. Phase III, randomised, double-blind, placebo-controlled study of the β3-adrenoceptor agonist mirabegron, 50 mg once daily, in Japanese patients with overactive bladder. *BJU Int.* 2014; **113**: 951–60.

192 Khullar V, Amarenco G, Angulo JC *et al*. Efficacy and tolerability of mirabegron, a β3-adrenoceptor agonist, in patients with overactive bladder: results from a randomised European-Australian phase 3 trial. *Eur. Urol.* 2013; **63**: 283–95.

193 Yoshida M, Takeda M, Gotoh M *et al*. Vibegron, a novel potent and selective β3-adrenoreceptor agonist, for the treatment of patients with overactive bladder: a randomized, double-blind, placebo-controlled phase 3 study. *Eur. Urol.* 2018; **73**: 783–90.

194 Yoshida M, Takeda M, Gotoh M *et al*. Efficacy of novel β3-adrenoreceptor agonist vibegron on nocturia in patients with overactive bladder: a post-hoc analysis of a randomized, double-blind, placebo-controlled phase 3 study. *Int. J. Urol.* 2019; **26**: 369–75.

195 Cardozo L, Lose G, McClish D, Versi E. A systematic review of the effects of estrogens for symptoms suggestive of overactive bladder. *Acta Obstet. Gynecol. Scand.* 2004; **83**: 892–7.

196 Abdelbary AM, El-Dessoukey AA, Massoud AM *et al*. Combined vaginal pelvic floor electrical stimulation (PFS) and local vaginal estrogen for treatment of overactive bladder (OAB) in perimenopausal females. Randomized controlled trial (RCT). *Urology* 2015; **86**: 482–6.

197 Fowler CJ, Auerbach S, Ginsberg D *et al*. OnabotulinumtoxinA improves health-related quality of life in patients with urinary incontinence due to idiopathic overactive bladder: a 36-week, double-blind, placebo-controlled, randomized, dose-ranging trial. *Eur. Urol.* 2012; **62**: 148–57.

198 Chapple C, Sievert K-D, MacDiarmid S *et al*. OnabotulinumtoxinA 100 U significantly improves all idiopathic overactive bladder symptoms and quality of life in patients with overactive bladder and urinary incontinence: a randomised, double-blind, placebo-controlled trial. *Eur. Urol.* 2013; **64**: 249–56.

199 Nitti VW, Dmochowski R, Herschorn S *et al*.; EMBARK Study Group. OnabotulinumtoxinA for the treatment of patients with overactive bladder and urinary incontinence: results of a phase 3, randomized, placebo controlled trial. *J. Urol.* 2013; **189**: 2186–93.

200 Cui YU, Wang L, Liu L *et al*. Botulinum toxin-A injections for idiopathic overactive bladder: a systematic review and meta-analysis. *Urol. Int.* 2013; **91**: 429–38.

201 Stewart F, Gameiro LF, El Dib R *et al*. Electrical stimulation with non-implanted electrodes for overactive bladder in adults. *Cochrane Database Syst. Rev.* 2016; (12): CD010098.

202 Correia GN, Pereira VS, Hirakawa HS, Driusso P. Effects of surface and intravaginal electrical stimulation in the treatment of women with stress urinary incontinence: randomized controlled trial. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 2014; **173**: 113–8.

203 Jha S, Walters SJ, Bortolami O *et al*. Impact of pelvic floor muscle training on sexual function of women with urinary incontinence and a comparison of electrical stimulation versus standard treatment (IPSU trial): a randomised controlled trial. *Physiotherapy* 2018; **104**: 91–7.

204 Lim R, Lee SWH, Tan PY *et al*. Efficacy of electromagnetic therapy for urinary incontinence: a systematic review. *Neurourol. Urodyn.* 2015; **34**: 713–22.

205 Lim R, Liong ML, Leong WS *et al*. Pulsed magnetic stimulation for stress urinary incontinence: 1-year followup results. *J. Urol.* 2017; **197**: 1302–8.

206 Yamanishi T, Suzuki T, Sato R *et al*. Effects of magnetic stimulation on urodynamic stress incontinence refractory to pelvic floor muscle training in a randomized sham-controlled study. *Low. Urin. Tract Symptoms* 2019; **11**: 61–5.

207 Siegel S, Noblett K, Mangel J *et al*. Results of a prospective, randomized, multicenter study evaluating sacral neuromodulation with InterStim therapy compared to standard medical therapy at 6-months in subjects with mild symptoms of overactive bladder. *Neurourol. Urodyn.* 2015; **34**: 224–30.

208 Amundsen CL, Richter HE, Menefee SA *et al*. OnabotulinumtoxinA vs sacral neuromodulation on refractory urgency urinary incontinence in women: a randomized clinical trial. *JAMA* 2016; **316**: 1366–74.

209 Amundsen CL, Komesu YM, Chermansky C *et al*.; Pelvic Floor Disorders Network. Two-year outcomes of sacral neuromodulation versus OnabotulinumtoxinA for refractory urgency urinary incontinence: a randomized trial. *Eur. Urol.* 2018; **74**: 66–73.

210 Booth J, Connelly L, Dickson S *et al*. The effectiveness of transcutaneous tibial nerve stimulation (TTNS) for adults with overactive bladder syndrome: a systematic review. *Neurourol. Urodyn.* 2018; **37**: 528–41.

211 Laurikainen E, Valpas A, Aukee P *et al*. Five-year results of a randomized trial comparing retropubic and transobturator midurethral slings for stress incontinence. *Eur. Urol.* 2014; **65**: 1109–14.

212 Ford AA, Rogerson L, Cody JD *et al*. Mid-urethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst. Rev.* 2017; **7**: CD006375.

213 Lo TS, Jaili S, Tan YL, Wu PY. Five-year follow-up study of Monarc transobturator tape for surgical treatment of primary stress urinary incontinence. *Int. Urogynecol. J.* 2016; **27**: 1653–9.

214 Xin X, Song Y, Xia Z. A comparison between adjustable single-incision sling and tension-free vaginal tape-obturator in treating stress urinary incontinence. *Arch. Gynecol. Obstet.* 2016; **293**: 457–63.

215 Abdel-Fattah M, Ford JA, Lim CP, Madhuvrata P. Single-incision mini-slings versus standard midurethral slings in surgical management of female stress urinary incontinence: a meta-analysis of effectiveness and complications. *Eur. Urol.* 2011; **60**: 468–80.

216 Nambiar A, Cody JD, Jeffery ST, Aluko P. Single-incision sling operations for urinary incontinence in women. *Cochrane Database Syst. Rev.*. 2017; (7): CD008709.

217 van der Ploeg JM, Oude Rengerink K, van der Steen A *et al*. Dutch Urogynaecology Consortium. Transvaginal prolapse repair with or without the addition of a midurethral sling in women with genital prolapse and stress urinary incontinence: a randomised trial. *BJOG* 2015; **122**: 1022–30.

218 Sharifiaghdas F, Mirzaei M, Daneshpajooh A, Narouie B. Long-term results of tension-free vaginal tape and pubovaginal sling in the treatment of stress urinary incontinence in female patients. *Clin. Exp. Obstet. Gynecol.* 2017; **44**: 44–7.

219 Khan ZA, Nambiar A, Morley R *et al*. Long-term follow-up of a multicentre randomised controlled trial comparing tension-free vaginal tape, xenograft and autologous fascial slings for the treatment of stress urinary incontinence in women. *BJU Int.* 2015; **115**: 968–77.

220 Rehman H, Bezerra CA, Bruschini H *et al*. Traditional suburethral sling operations for urinary incontinence in women. *Cochrane Database Syst. Rev.* 2017; (7): CD001754.

221 Osman NI, Hillary CJ, Mangera A *et al*. The midurethral fascial "sling on a string": an alternative to midurethral synthetic tapes in the era of mesh complications. *Eur. Urol.* 2018; **74**: 191–6.

222 Lapitan MCM, Cody JD, Mashayekhi A. Open retropubic colposuspension for urinary incontinence in women. *Cochrane Database Syst. Rev.* 2017; (7): CD002912.

223 Valpas A, Ala-Nissilä S, Tomas E, Nilsson CG. TVT versus laparoscopic mesh colposuspension: 5-year follow-up results of a randomized clinical trial. *Int. Urogynecol. J.* 2015; **26**: 57–63.

224 Dean N, Ellis G, Herbison GP *et al*. Laparoscopic colposuspension for urinary incontinence in women. *Cochrane Database Syst. Rev.* 2017; (7): CD002239.

225 Glazener CM, Cooper K, Mashayekhi A. Anterior vaginal repair for urinary incontinence in women. *Cochrane Database Syst. Rev.* 2017; (7): CD001755.

226 Glazener CM, Cooper K, Mashayekhi A. Bladder neck needle suspension for urinary incontinence in women. *Cochrane Database Syst. Rev.* 2017; (7): CD003636.

227 Kirchin V, Page T, Keegan PE *et al*. Urethral injection therapy for urinary incontinence in women. *Cochrane Database Syst. Rev.* 2017; (7): CD003881.

228 Phé V, Benadiba S, Rouprêt M *et al*. Long-term functional outcomes after artificial urinary sphincter implantation in women with stress urinary incontinence. *BJU Int.* 2014; **113**: 961–7.

229 Phé V, Léon P, Granger B *et al*. Stress urinary incontinence in female neurological patients: long-term functional outcomes after artificial urinary sphincter (AMS 800TM) implantation. *Neurourol. Urodyn.* 2017; **36**: 764–9.

230 Peyronnet B, Vincendeau S, Tondut L *et al*. Artificial urinary sphincter implantation in women with stress urinary incontinence: preliminary comparison of robot-assisted and open approaches. *Int. Urogynecol. J.* 2016; **27**: 475–81.

231 Shreck E, Gioia K, Lucioni A. Indications for augmentation cystoplasty in the era of onabotulinumtoxinA. *Curr. Urol. Rep.* 2016; **17**: 27.

232 Di Pierdomenico AA, Radomski SB. Success rates of patients with poor emptying on clean intermittent catheterization. *Can. J. Urol.* 2014; **21**: 7188–93.