Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline Amendment

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Abbreviations and Acronyms

AE = adverse event

AHRQ = Agency for Healthcare Research and Quality

FDA = U.S. Food and Drug Administration

OAB = overactive bladder

PTNS = peripheral tibial nerve stimulation

PVR = post-void residual

QoL = quality of life

SNS = sacral neuromodulation

UTI = urinary tract infection

UUI = urgency urinary incontinence

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For another article on a related topic see page 1692.

Purpose: The purpose of this guideline amendment, herein referred to as the amendment, is to incorporate relevant newly published literature to better provide a clinical framework for the diagnosis and treatment of patients with non-neurogenic overactive bladder.

Materials and Methods: The primary source of evidence for this guideline is the systematic review and data extraction conducted as part of the Agency for Healthcare Research and Quality Evidence Report/Technology Assessment Number 187 titled Treatment of Overactive Bladder in Women (2009). That report searched PubMed, MEDLINE®, EMBASE and CINAHL for English language studies published from January 1966 to October 2008. The AUA conducted additional literature searches to capture populations and treatments not covered in detail by the AHRQ report and relevant articles published through December 2011. The review yielded 151 treatment articles after application of inclusion/exclusion criteria. An additional systematic review conducted in February 2014 identified 72 additional articles relevant to treatment and made up the basis for the 2014 amendment.

Results: The amendment focused on four topic areas: mirabegron, peripheral tibial nerve stimulation, sacral neuromodulation and BTX-A. The additional literature provided the basis for an update of current guideline statements as well as the incorporation of new guideline statements related to the overall management of adults with OAB symptoms.

Conclusions: New evidence-based statements and expert opinion supplement the original guideline published in 2012, which provided guidance for the diagnosis and overall management of OAB in adults. An integrated presentation of the OAB guideline with the current amendments is available at www.auanet.org.

Key Words: urinary bladder, urinary incontinence, nocturia

INTRODUCTION

The purpose of this guideline is to direct specialist and non-specialist clinicians and educate patients regarding how to recognize non-neurogenic overactive bladder, conduct a valid diagnostic process and establish treatment goals that maximize symptom control and patient quality of life while minimizing adverse events and patient burden. The strategies and approaches discussed in this document were derived from evidence-based and consensus-based processes derived from a continually expanding body of literature on OAB. The Panel notes that this document constitutes a clinical strategy and is not intended to be

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interpreted rigidly. The most effective approach for a particular patient is best determined by the individual clinician and patient. As the science relevant to OAB evolves and improves, this guideline amendment assures the highest contemporary clinical practices. The strategies presented here will require further amendment to remain consistent with the highest standards of clinical care.

METHODOLOGY

The primary source of evidence for the original version of this guideline published in 2012 was the systematic review and data extraction conducted as part of the AHRQ Evidence Report/Technology Assessment Number 187.[1] That report searched PubMed, MEDLINE®, EMBASE and CINAHL for English language studies published from January 1966 to October 2008 relevant to OAB and excluded non-relevant studies, studies with fewer than 50 participants and studies with fewer than 75% women. AUA conducted an additional literature search to capture articles published through December 2011. This search included studies on men and nocturia which had been excluded in the AHRQ report. Given that the AHRQ report included limited information regarding use of neuromodulation therapies, including sacral neuromodulation and peripheral tibial nerve stimulation (also known as posterior tibial nerve stimulation), and limited information on the use of intravesical onabotulinumtoxinA to treat non-neurogenic OAB, additional searches were performed to capture this literature up to December 2011.

In February 2014 the OAB guideline was updated through the AUA amendment process in which newly published literature is reviewed and integrated into previously published guidelines in an effort to maintain currency. AUA's amendment process provides for the amendment of existing evidence-based guideline statements and/or the creation of new evidence-based guideline statements in response to the publication of a sufficient volume of new evidence. The amendment focused on four topic areas: mirabegron, PTNS, SNS and BTX-A. This review identified an additional 72 articles relevant to treatment published from January 2012 to Feb 2014. These articles were added to the database, and AUA's qualitative and quantitative analyses were updated as appropriate. Data from studies published after the literature search cut-off will be incorporated into the next version of this guideline. For a complete discussion of the methodology and evidence grading, please refer to the full-length version of this guideline available at http://www.auanet.org/content/media/OAB_guideline.pdf.

BACKGROUND

OAB is a clinical diagnosis defined by the International Continence Society as the presence of "urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence (UUI), in the absence of a urinary tract infection (UTI) or other obvious pathology."[2] Methodological differences across studies challenge any interpretation of the OAB literature related to epidemiology and treatment. Most studies of OAB, including this guideline, exclude individuals with symptoms related to neurologic conditions.

Symptoms

When urinary frequency (daytime and nighttime) and urgency, with or without urgency incontinence, in the absence of UTI or other obvious pathology is self-reported as bothersome, the patient may be diagnosed with OAB.[3]

Differentiation

The differential of nocturia includes nocturnal polyuria, low nocturnal bladder capacity or both. In nocturnal polyuria, nocturnal voids are frequently normal or large volume as opposed to the small volume voids commonly observed in nocturia associated with OAB. Sleep disturbances, vascular and/or cardiac disease and other medical conditions are often associated with nocturnal polyuria.

Frequency that is the result of polydipsia and resulting polyuria may mimic OAB; the two are distinguished with the use of frequency-volume charts. Polydipsia-related frequency is physiologically self-induced and should be managed with education and consideration of fluid management.

While the clinical presentation of interstitial cystitis/ bladder pain syndrome shares the symptoms of frequency and urgency with OAB, bladder and/or pelvic pain, including dyspareunia, is a crucial component of its presentation in contradistinction to OAB. A summary algorithm of the diagnosis and treatment of OAB can be found in the Figure.

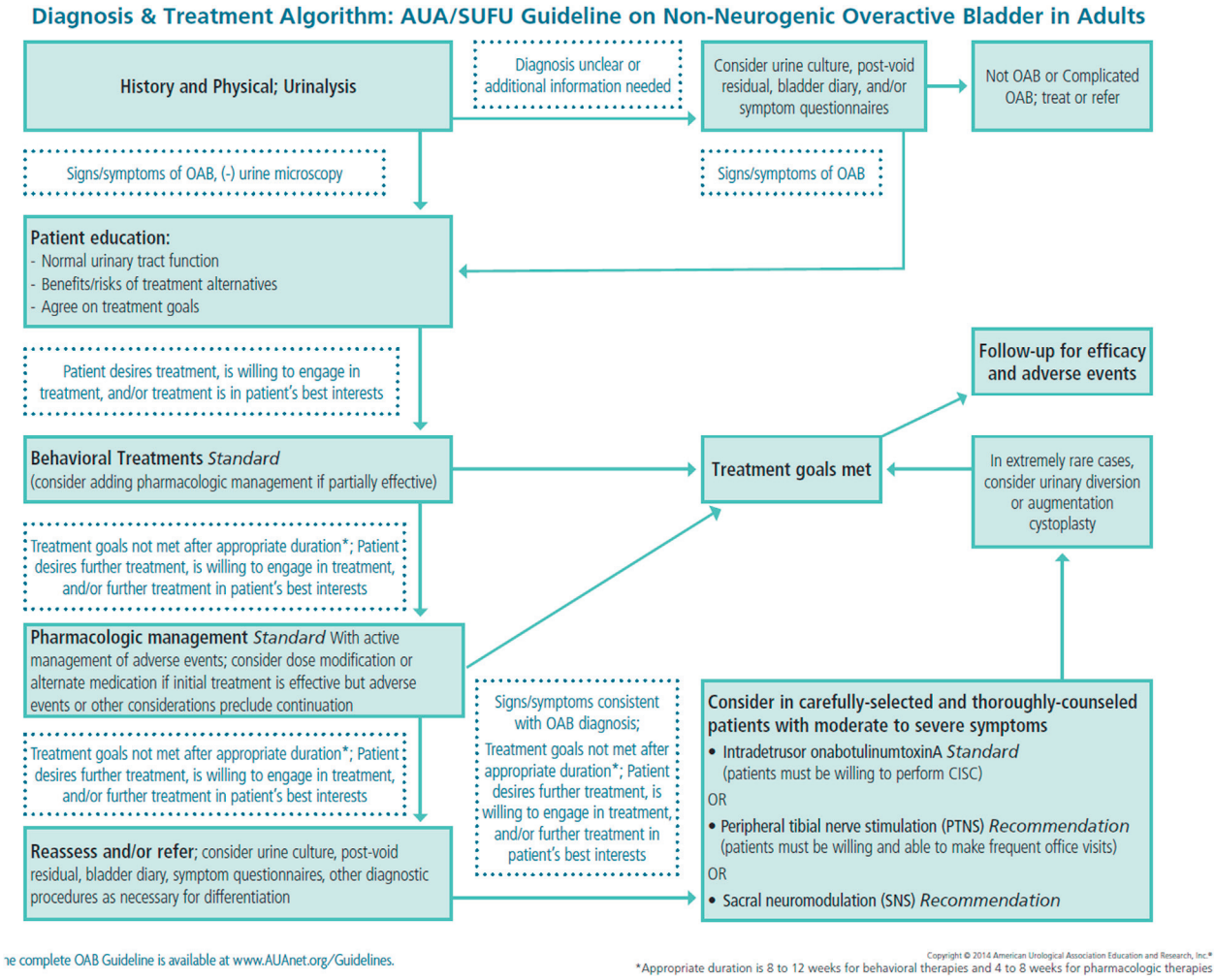
GUIDELINE AMENDMENTS

Diagnosis

The 2014 amendment search failed to identify additional literature relevant to OAB diagnosis to provide evidence-based support for the guideline statements. As such, the statements related to diagnosis remain unchanged from the 2012 release of the original guideline.

Treatment

It is important to recognize that OAB is a symptom complex that may compromise QoL but generally does not affect survival. Given this context, in pursuing a treatment plan the clinician should carefully weigh the potential benefit to the patient of a particular treatment against that treatment's risk for AEs, the severity of adverse events and the reversibility of AEs. The guideline statements in



Diagnosis and treatment algorithm

this section are intended to provide a framework to assist the clinician in counseling patients and in developing an individualized treatment plan that optimizes QoL. Overactive bladder symptoms are rarely cured, but often the symptoms and burden on QoL can be ameliorated.

The Panel conceptualized risks/burdens in terms of the invasiveness of the treatment, the duration and severity of potential AEs, and the reversibility of potential AEs. Treatments were then divided into first-, second- and third-line groups. This hierarchy was derived by balancing the potential benefits to the patient with the invasiveness of the treatment, the duration and severity of potential AEs, and the reversibility of potential AEs. First-line treatment with behavioral therapy presents essentially no risks to patients and should be offered to all patients. Second-line treatment with pharmaceutical agents is not invasive and presents the risk of side effects that primarily compromise QoL. Any AEs are readily reversible with cessation of the medication. Third-line treatment with intradetrusor onabotulinumtoxinA or sacral neuromodulation is invasive and has risks. PTNS has minimal risks but requires a very motivated patient who can make multiple visits in a short period of time. Additional treatments, including major surgical procedures, such as bladder augmentation, have greater risks and are irreversible.

First-line treatments: behavioral therapies. **Guideline Statement 7:** "Behavioral therapies may be combined with pharmacologic management." ***(Recommendation*; *Evidence Strength: Grade C)***

Behavioral and drug therapies are often used in combination in clinical practice to optimize patient symptom control and QoL. A limited literature indicates that initiating behavioral and drug therapy simultaneously may improve outcomes, including frequency, voided volume, incontinence and symptom distress.[4–8] The use of "pharmacologic

management" in the 2014 amendment includes β_3-adrenoceptor agonists and anti-muscarinics as suitable choices for pharmaceutical treatment of OAB. In the Panel's judgment there are no known contraindications to combining pharmacologic management and behavioral therapies.

Second-line treatments: pharmacologic management. **Guideline Statement 8:** "Clinicians should offer oral anti-muscarinics or oral β_3-adrenoceptor agonists as second-line therapy." ***(Standard; Evidence Strength: Grade B)***

The amendment search retrieved a newly published set of studies that evaluated the benefits and risks/burdens of mirabegron, a β_3-adrenoceptor agonist. Seven studies evaluated mirabegron in comparison to a placebo group and/or an active control group[9–15] in a total of 9,310 patients; 5,884 of these patients were in the mirabegron groups. For the five studies that used an active control group, the active control was tolterodine ER 4 mg. Five studies were Phase III trials evaluating safety and efficacy. One study was a Phase II proof-of-concept study[15] and one study was a Phase II dose-ranging trial.[14] Five studies followed patients for 12 weeks. The proof-of-concept study followed patients for four weeks.[15] One of the Phase III trials followed patients for one year.[12]

Significant improvements in mean voided volume/micturition, mean level of urgency, mean number of urgency episodes (grade 3 or 4)/day, mean number UUI episodes per day and mean number nocturia episodes per day also were noted for both doses compared to placebo. The proportion of patients reporting zero incontinence episodes was significantly higher in the mirabegron groups (50 mg: 44.1%; 100 mg: 46.4%) compared to placebo (37.8%). Efficacy in patients who had used anti-muscarinics compared to treatment-naïve patients was similar across doses. The 25 mg dose significantly reduced frequency and incontinence episodes but generally not other end points. The 50 and 100 mg doses also significantly improved ratings on the Treatment Satisfaction-VAS compared to placebo. There was no dose-response gradient for the 50 mg dose compared to the 100 mg dose with both doses producing similar effects.

Overall, the Panel interpreted the mirabegron data to indicate that mirabegron appears to be similar in efficacy to the anti-muscarinics and has lower rates of dry mouth than any of these medications. Mirabegron produces lower rates of constipation than some of the anti-muscarinics. This lower incidence of bothersome AEs may inform the selection of medications for patients who already present with dry mouth (e.g., secondary to Sjogren's syndrome) and/or constipation or for patients who experience efficacy from the anti-muscarinics but cannot tolerate the associated AEs.

Guideline Statement 11: "If a patient experiences inadequate symptom control and/or unacceptable adverse drug events with one anti-muscarinic medication, then a dose modification or a different anti-muscarinic medication or a β_3-adrenoceptor agonist may be tried." ***(Clinical Principle)***

In the Panel's experience, patients who experience inadequate symptom control and/or unacceptable adverse drug events with one anti-muscarinic medication may experience better symptom control and/or a more acceptable adverse drug event profile with another anti-muscarinic or with a β_3-adrenoceptor agonist. In addition, in some patients, dose modification (i.e., reducing dose or reducing dose and combining medication with behavioral techniques) may achieve a better balance between efficacy and adverse drug events. A small literature composed of observational studies supports this experience, particularly when switching from an immediate release medication to a newer sustained release medication. Based on the Panel's clinical experience and this limited literature, the Panel advises that clinicians should not abandon anti-muscarinic therapy if trial of one medication appears to fail or produces an unacceptable AE profile. Further, clinicians may also switch patients to a β_3-adrenoceptor agonist (e.g., mirabegron) given an efficacy profile that appears similar to the anti-muscarinics and a relatively lower AE profile.

There is no literature that addresses combination therapy of anti-muscarinics with each other. There are limited studies addressing the combination of the anti-muscarinics with β_3-adrenoceptor agonists. While there is literature on the combination of anti-muscarinics with other classes of medication, such as tricyclics to manage neurogenic OAB, this literature may not be applicable to the non-neurogenic OAB population.

Guideline Statement 15: "Clinicians should use caution in prescribing anti-muscarinics or β_3-adrenoceptor agonists in the frail OAB patient." ***(Clinical Principle)***

In frail patients, defined as patients with mobility deficits (i.e., require support to walk, have slow gait speed, have difficulty rising from sitting to standing without assistance), weight loss and weakness without medical cause, and who may have cognitive deficits,[16] the use of OAB medications may have a lower therapeutic index and a higher adverse drug event profile. The Panel notes that presently there are no data on the use of β_3-adrenoceptor agonists (e.g., mirabegron) in the frail patient, the patient with significant comorbidities or the patient on multiple medications. In patients who cannot

tolerate anti-muscarinics or for whom pharmacologic management is not appropriate, behavioral strategies that include prompted voiding and fluid management may be helpful.

Guideline Statement 16: "Patients who are refractory to behavioral and pharmacologic therapy should be evaluated by an appropriate specialist if they desire additional therapy." ***(Expert Opinion)***

The Panel defines the refractory patient as the patient who has failed a trial of symptom-appropriate behavioral therapy of sufficient length, 8 to 12 weeks, to evaluate potential efficacy and who has failed a trial of at least one anti-muscarinic medication administered for 4 to 8 weeks. Failure of an anti-muscarinic medication may include lack of efficacy and/or inability to tolerate adverse drug effects. The Panel notes that this definition is a minimum definition; individual clinicians and patients may decide that it is in the best interests of the patient to persevere with behavioral and/or pharmacologic therapy for longer periods, to combine behavioral and pharmacologic therapies or to use combinations of pharmacologic therapies to achieve better efficacy, or to try alternate medications before judging that a patient is refractory.

Third-line treatments. The Panel notes that the use of all third-line therapies requires careful patient selection and appropriate patient counseling. There is no literature that addresses using these therapies in combination.

Guideline Statement 17: "Clinicians may offer intradetrusor onabotulinumtoxinA (100 U) as third-line treatment in the carefully-selected and thoroughly-counseled patient who has been refractory to first- and second-line OAB treatments. The patient must be able and willing to return for frequent post-void residual (PVR) evaluation and able and willing to perform self-catheterization if necessary." ***(Standard; Evidence Strength: Grade B)***

The Panel upgraded intradetrusor onabotulinumtoxinA treatment from an Option to a Standard in the thoroughly educated and carefully counseled patient with moderate to severe OAB symptoms because a body of moderate quality evidence indicated that sustained improvements in voiding, QoL outcomes and rates of AEs that could compromise QoL or lead to serious illness were less likely to occur with use of the FDA approved dose of 100 U.

The amendment search retrieved 27 new studies, including five randomized trials with placebo control groups[10,17–20] and two randomized trials with active control.[21] The lack of long-term follow-up remains, with the largest trials reporting outcomes at 12 weeks. In contrast to prior evidence, the most commonly used dose was 100 U rather than 200 U.

Fowler et al[22] reported QoL data from the Dmochowski et al[23] dose-finding trial and noted that the I-QoL and Kings Health Questionnaire exhibited significant improvement compared to placebo for all groups administered 100 U or greater. Studies that measured urodynamic parameters also reported improvements (e.g., in maximum bladder capacity). Denys et al compared placebo to 50 U, 100 U and 150 U.[18] At three months post-procedure, >50% improvement in urgency and UUI was reported by 30% of placebo patients, 37% of the 50 U patients, 68% of 100 U patients and 58% of 150 U patients (sample sizes were <30 in each group; only the 100 U group was statistically significantly different from placebo). The 100 U and 150 U groups exhibited significantly reduced frequency compared to placebo and this reduction persisted for 30 days in the 100 U group and was still significant at 60 months for the 150 U group. The number of patients who achieved complete continence at three months was significantly greater in the 100 U group (55%) and the 150 U group (50%) compared to the placebo group (11%). At five months post-treatment, these differences were maintained.

These outcomes occurred, however, in the context of high rates of AEs in the active treatment groups in some studies. Rates of UTIs ranged from 3.6% to 54.5% with four of the RCTs reporting rates of >40.0% and Dmochowski et al reporting that rates generally increased with dose with rates ranging from 33.9% to 48.1% across active treatment groups.[23] Rates of urinary retention were reported in 10 studies and ranged from 0% to 43% with rates of 43.0% and 30.0% reported in one RCT (elevated PVR defined as 200 cc)[24] and one observational study (elevated PVR defined as 250 cc),[25] respectively.

Bauer et al focused more broadly on side effects and interviewed patients (n = 56) who had been administered onabotulinumtoxinA (100, 150 or 200 U) or abobotulinumtoxinA (500 U) regarding the occurrence of gross hematuria, dry mouth, dysphagia, speech problems, impaired vision and weakness of the eyelids, arms, legs, torso and/or whole body.[26] Approximately 54% of patients reported at least one side effect, including urinary retention (8.9%), gross hematuria (17.9%), UTI (7.1%), dry mouth (19.6%), dysphagia (5.4%), impaired vision (5.4%), eyelid weakness (8.9%), arm weakness (8.9%), leg weakness (7.1%) and torso weakness (5.4%). The authors note that symptoms other than urinary retention and UTI were transient, and resolved without the need for further treatment.

The Panel interpreted these data to indicate that onabotulinumtoxinA injections can improve

moderate to severe OAB symptoms in the context of AEs that could require secondary intervention (e.g., an untreated UTI, urinary retention that requires clean intermittent catheterization). The Panel notes that at the FDA approved dose of 100 U some AEs appear to occur less frequently. Patients considering onabotulinumtoxinA treatment must be counseled regarding the possible need to perform self-catheterization for long periods (or to have a caregiver perform catheterization) and should be willing to accept this possibility. Further, effects diminish over time for most patients; therefore, patients also should be informed that repeat injections are likely to be necessary to maintain symptom reduction.

Guideline Statement 18: "Clinicians may offer peripheral tibial nerve stimulation (PTNS) as third-line treatment in a carefully selected patient population." ***(Recommendation; Evidence Strength: Grade C)***

The amendment search retrieved eleven new publications that reported outcomes from nine studies, including one RCT,[27] and one randomized design.[28] Although most studies reported outcomes at 12 weeks, several reported longer-term findings. Peters (2013a, 2013b) reported findings in a group of responders from the SUmiT trial who continued with PTNS therapy for up to 36 months.[29,30] Yoong (2013) reported one-year findings for a group of PTNS responders.[31] Several other papers reported partial findings beyond the formal study end date. Sample sizes remained relatively small (range 14 to 60 patients) with most studies having fewer than 25 patients in each treatment arm.

In Souto (2014), patients were randomized to three groups: PTNS, oxybutynin ER 10 mg/daily, and PTNS + oxybutynin ER 10 mg/daily.[28] PTNS patients had treatments twice a week, for 30 min, for 12 weeks. At 12 weeks, all three groups showed similar improvements in frequency, incontinence, nocturia, ICIQ-SF scores, ICIQ-OAB scores, and symptom bother scores. The authors followed patients after treatment cessation for another 12 weeks. At week 24, the oxybutynin group had significantly worse scores compared to week 12 on the QoL measures − but not the two groups that had PTNS. Frequency, incontinence, and nocturia data at 24 weeks were only reported as proportions of patients exhibiting these symptoms; it appears that the oxybutynin only group had decaying responses compared to the PTNS groups.

The Panel interpreted these data to indicate that PTNS can benefit a carefully selected group of patients characterized by moderately severe baseline incontinence and frequency and willingness to comply with the PTNS protocol. Patients must also have the resources to make frequent office visits both during the initial treatment phase and to obtain maintenance treatments in order to achieve and maintain treatment effects. Reported AEs were minor; the most frequently reported events were painful sensation during stimulation that did not interfere with treatment and minor bleeding at the insertion site.

Guideline Statement 19: "Clinicians may offer sacral neuromodulation (SNS) as third-line treatment in a carefully selected patient population characterized by severe refractory OAB symptoms or patients who are not candidates for second-line therapy and are willing to undergo a surgical procedure." ***(Recommendation; Evidence Strength: Grade C)***

The amendment search retrieved an additional 16 relevant treatment studies, including one prospective randomized multi-center trial,[32] one crossover study[33] and 14 observational studies. Seigel et al reported findings at six months of follow-up for the InSite trial, an ongoing FDA mandated post-device approval study that included a subsample of patients randomized to SNS or to standard medical therapy (anti-muscarinic medications).[32] The study used the newer tined lead. A total of 147 patients were randomized (SNS 70, SMT 77) and 130 patients completed six months of treatment (SNS 59, SMT 71).

Patients in the Seigel et al study had less severe symptom levels at baseline (SNS: mean 11.2 voids/day, mean 2.4 incontinence episodes/day, mean 1.1 pads/day; SMT: mean 11.9 voids/day, mean 2.7 incontinence episodes/day. mean 1.5 pads/day).[32] In addition, the primary outcome was OAB therapeutic success defined as $\geq$50% improvement in average incontinence episodes/day or voids/day or a return to normal voiding frequency of $<$8 voids/day rather than change in voids or incontinence episodes. At 6 months, the OAB success rate was 61% in the SNS group compared to 42% in the SMT group ($p=0.02$). In addition, $<$8 voids/day was achieved by 61% of SNS patients compared to 37% of SMT patients ($p=0.04$). The SNS group also improved more in OAB-QoL than did the SMT group ($p<0.001$), SNS female patients reported a greater improvement in sexual function than did SMT female patients ($p<0.05$) and the SNS group exhibited greater improvements in Beck Depression Inventory scores than did the SMT group ($p=0.01$).

The crossover study evaluated whether different stimulator settings altered outcomes.[33] Patients in this study had had an SNS implant with a tined lead for at least three months prior to the start of the study and were refractory to conventional treatments including medications at the time of SNS implant. Rate settings were 5.2 Hz, 14 Hz or 25 Hz and were maintained for one week. Numbers

of incontinence episodes and pad changes were significantly affected by rate such that the 14 Hz and 25 Hz settings reduced these outcomes compared to the 5.2 Hz setting.

The Panel interpreted these data to indicate that in carefully selected patients, SNS is an appropriate therapy that can have durable treatment effects but in the context of frequent and moderately severe AEs, including the need for additional surgeries. The Panel notes that patients should be counseled that the device requires periodic replacement in a planned surgical procedure and that the length of time between replacements depends on device settings and usage. Patients also must be willing to comply with the treatment protocol because treatment effects typically are only maintained as long as the therapy is maintained. Patients must have the cognitive capacity to use the remote control to optimize device function. In addition, patients must accept that the use of diagnostic magnetic resonance imaging below the head is contraindicated in individuals with the device implanted.

Guideline Statement 20: "Practitioners and patients should persist with new treatments for an adequate trial in order to determine whether the therapy is efficacious and tolerable. Combination therapeutic approaches should be assembled methodically, with the addition of new therapies occurring only when the relative efficacy of the preceding therapy is known. Therapies that do not demonstrate efficacy after an adequate trial should be ceased." ***(Expert Opinion)***

The Panel notes that they regularly encounter patients who present for more burdensome second- or third-line treatments who have never undergone a comprehensive evaluation (i.e., completion of a voiding diary to ensure the OAB diagnosis is correct) and/or who have never had an adequate first-line trial of behavioral therapy . Similarly, it is not uncommon for patients to present for third-line treatments who have had an inadequately managed trial of medications (e.g., short trials, or lack of dose modification or of supportive management for commonly associated side effects). On the other hand, the Panel also encounters patients who are being treated with multiple simultaneous second- and third-line therapies without clear evidence of efficacy of any individual therapy or the establishment of realistic and shared goals of treatment.

The Panel encourages practitioners and patients to persist with new treatments (4 to 8 weeks for medications and 8 to 12 weeks for behavioral therapies) for a sufficient duration to achieve clarity regarding efficacy and AEs for a particular therapy before abandoning the therapy prematurely or before adding a second therapy. If a comprehensive evaluation has demonstrated that the patient has signs and symptoms consistent with the OAB diagnosis and a particular therapy is not efficacious after a reasonable trial, then an alternative therapy should be tried, should the patient so desire. Combination therapeutic approaches should be assembled methodically, beginning with the establishment of confidence in the partial efficacy of one therapy, continuing with an adequate trial of any additional therapies one at a time until the patient experiences adequate symptom control in the context of tolerable AEs. If a patient does not achieve adequate symptom control with this approach, then referral to a specialist should be considered.

RESEARCH NEEDS AND FUTURE DIRECTIONS

The Panel recognizes that much additional research is needed for OAB including epidemiologic, basic science, translational and clinical research. For a detailed description of research needs and future directions please refer to the full-length version of this guideline.

PANEL ACKNOWLEDGEMENT

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Disclaimer

The original version of this Overactive Bladder Guideline was created in 2009 by a multidisciplinary Panel assembled by the Practice Guidelines Committee (PGC) of the American Urological Association Education and Research, Inc. (AUA). This amended Overactive Bladder Guideline, drafted in 2014 by a subset of the original Overactive Bladder Guideline Panel. This amendment updates the original guideline document to reflect literature released following the original publication.

The mission of the original and amendment Panels was to develop clinical guideline recommendations based on an in-depth evidence report of the peer-reviewed literature. The recommendations are based on evidence strength, or where evidence is not available, on Delphi-modification consensus statements. The purpose of each guideline is to provide physicians and non-physician providers

(primary care and specialists) with a consensus of principles and treatment plans for the management of overactive bladder. While these guidelines do not necessarily establish the standard of care, AUA seeks to recommend and to encourage compliance by practitioners with current best practices related to the condition being treated.

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As medical knowledge expands and technology advances, AUA guidelines are subject to change. Evidence-based guideline statements are not absolute mandates but thoroughly considered strategies for best practice under the specific conditions described in each document. For all these reasons, the guidelines do not pre-empt physician judgment in individual cases. Treating physicians must take into account variations in resources, and patient tolerances, needs, and preferences. Similarly, conformance with any clinical guideline cannot assure a successful outcome. These guidelines and best practice statements are not intended to provide legal advice

The guideline text may include information or recommendations about certain drug or device use ('off label') that are not approved by the Food and Drug Administration (FDA), or about medications or substances not subject to the FDA approval process. AUA urges strict compliance with all government regulations and protocols for prescription and use of these substances. The physician is encouraged to understand and carefully follow all available prescribing information about indications, contraindications, precautions and warnings.

Although guidelines are intended to encourage best practices and to reflect available technologies with sufficient data as of the date of close of the literature review, guidelines are necessarily time-limited. Guidelines cannot include evaluation of all data on emerging technologies, pharmaceuticals or management practices, including both those that are FDA-approved, or those which may immediately come to represent accepted clinical practices. For this reason, the AUA does not regard emerging technologies or management techniques not addressed by this guideline as manifestly experimental or investigational. These emerging technologies or techniques may simply be too new to be included or fully incorporated in the Panel's evidence-based evaluation at the time the guideline is developed.

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