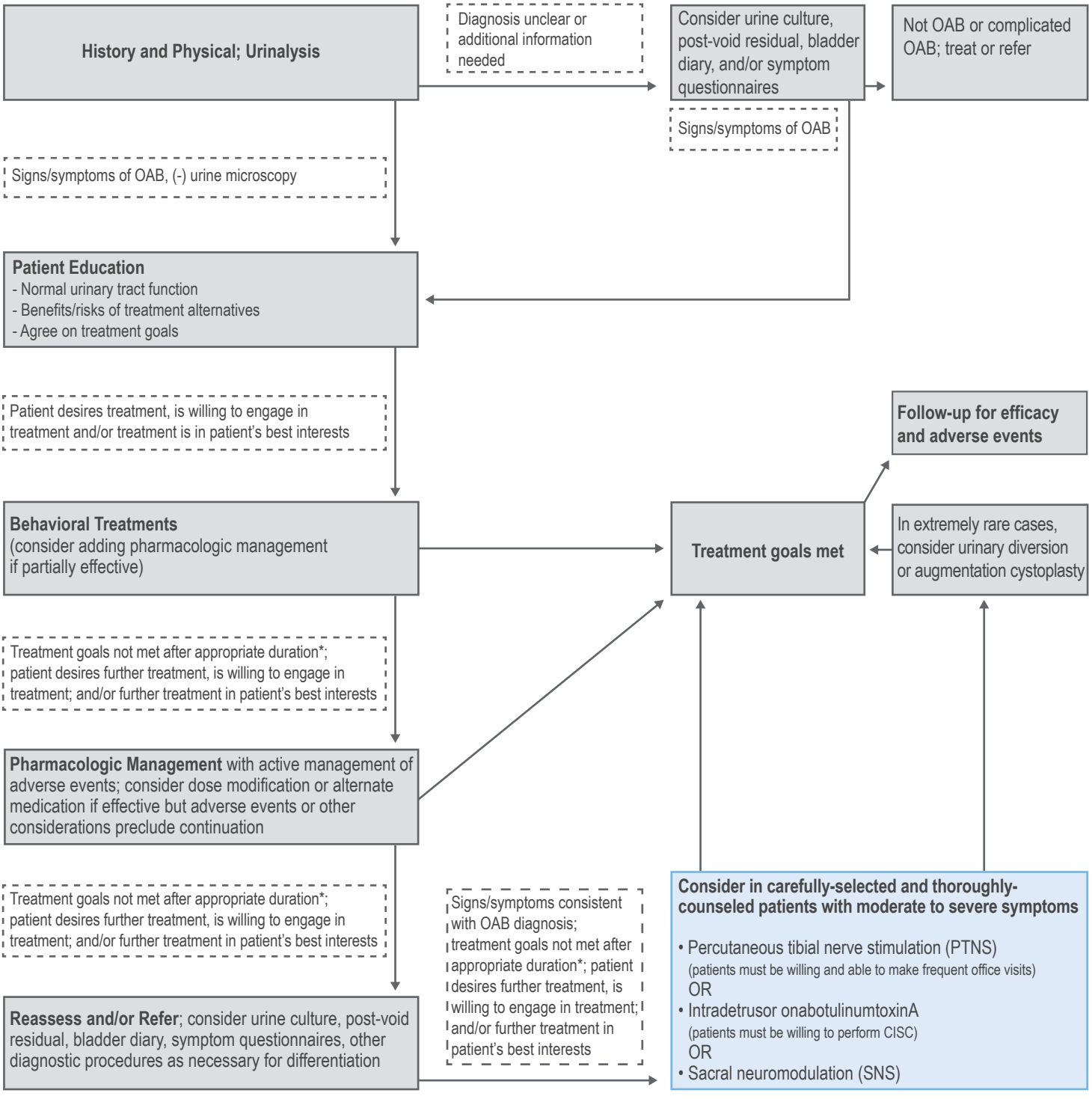
Overactive Bladder

DIAGNOSIS AND TREATMENT

Non-Neurogenic OAB Treatment in Adults Based on AUA/SUFU Guideline Algorithm[1]



*Appropriate duration is 8 – 12 weeks for behavioral therapies; 4 – 8 weeks for pharmacologic therapies

TREATING THE REFRACTORY OAB PATIENT

Summarized from the AUA/SUFU Guideline for the Diagnosis and Treatment of Overactive Bladder[2]

THE REFRACTORY PATIENT

- Failed a 8 – 12 week trial of symptom appropriate behavioral therapy
- Failed a 4 – 8 week trial of at least one pharmacologic therapy
- Failure is based on efficacy and/or inability to tolerate adverse effects

TREATING THE REFRACTORY PATIENT

- Some patients and clinicians may choose to try additional combinations of drugs and behavioral therapies before considering third-line therapies
- Third-line treatments done at the specialist level
- Clinicians may offer the third-line treatments in any order
- 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 adequate trial should be ceased
- No literature addresses using third-line treatments in combination

PERCUTANEOUS TIBIAL NERVE STIMULATION
Urgent® PC Neuromodulation System

GUIDELINE STATEMENT 18:

"Clinicians may offer [percutaneous] tibial nerve stimulation (PTNS) as third-line treatment in a carefully selected patient population."

PATIENTS UNDERGOING PTNS SHOULD:

- Have moderately severe baseline incontinence and frequency
- Be willing to comply with the PTNS protocol
- Have the resources to make frequent office visits, during initial treatment phase and to obtain maintenance treatments

INTRADETRUSOR ONABOTULINUMTOXINA
BOTOX®

Guideline Statement 17:

"Clinicians may offer intradetrusor onabotulinumtoxinA (100U) 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 evaluation and able and willing to perform self-catheterization if necessary."

Patient undergoing intradetrusor onabotulinumtoxinA should:

- Accept the possibility of performing self-catheterization for long periods (or to have a caregiver perform catheterization)
- Have access to a clinician who can measure PVR on a periodic basis if necessary
- Accept that repeat injections are likely to be necessary to maintain symptom reduction

SACRAL NERVE STIMULATION
InterStim®

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."

Patients undergoing SNS should:

- Understand that SNS can have durable effects but in the context of frequent and moderately severe adverse events, including the need for additional surgeries
- Accept that SNS requires periodic device replacement in planned surgical procedures, frequency on which is based on device settings
- Be willing to comply with SNS protocol
- Have the cognitive capacity to use the remote control to optimize device function
- Accept that use of diagnostic MRIs is contraindicated

CLINICAL REVIEW OF 3RD LINE OAB TREATMENTS

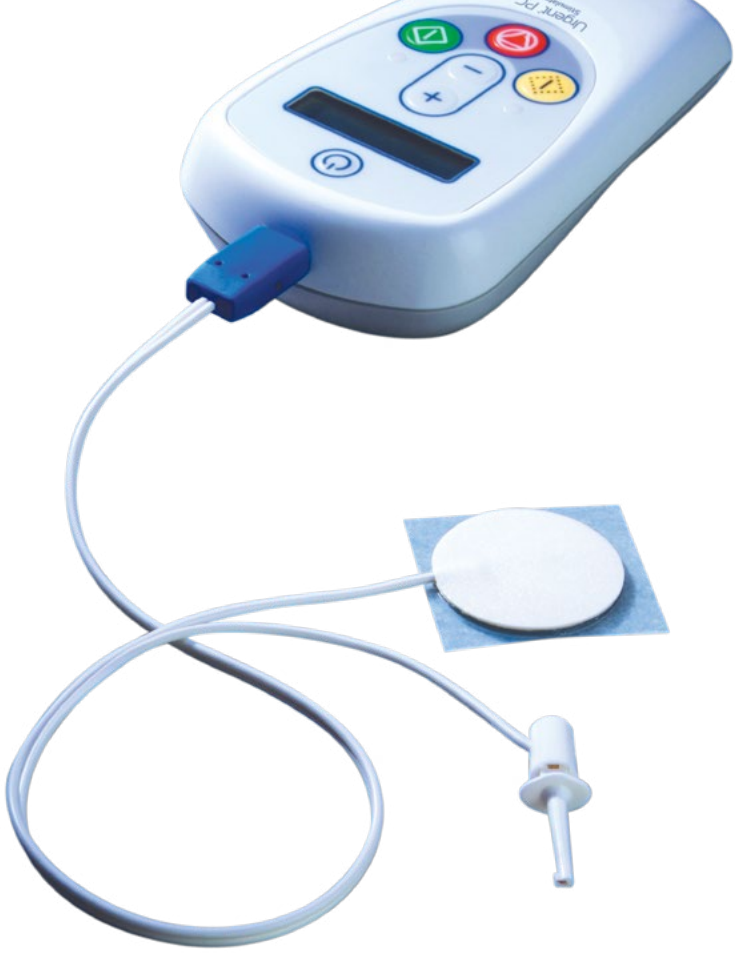
Summarized from the AUA/SUFU Guideline for the Diagnosis and Treatment of Overactive Bladder[2]

Therapy	Percutaneous Tibial Nerve Stimulation	Intradetrusor onabotulinumtoxinA (100U)	Sacral Nerve Stimulation
Brand Name	Urgent® PC	BOTOX®	InterStim®
Patient Group	» Refractory OAB symptoms with moderately severe baseline levels of incontinence and frequency	» Refractory OAB symptoms; varying baseline	» Extremely severe baseline incontinence and frequency; more than 4 pads used per day
Clinical Results	» Most studies show improvements in all measured symptoms including incontinence, frequency, nocturia and QoL » PTNS effects are similar in magnitude to anti-muscarinics » PTNS superior to Sham treatment	» Most trials reported statistically significant improvement in measured voiding outcomes and in QoL outcomes compared to placebo groups.	» Most studies show improvements in all measured parameters including QoL and subjective improvement » Improvement dissipates if treatment ceases » Favorable results compared to antimuscarnicis
Durability	» Durable results shown through 36 months with an average of 1 treatment per month after the initial treatment phase.	» Improvements deteriorate in majority of patients after 6 – 9 months	» Improvements sustained for 5 years in 56 – 68% of implanted patients
Adverse Events	"Reported adverse events 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."	"… outcomes occurred … in the context of high adverse events in the active treatment groups in some studies." » Rates of UTIs ranged from 3.6 – 54.5%; 4 RTCs reported rates of >40% » Urinary retention reported in 10 studies and ranged from 0 – 43% (rates of 43% and 30% in one RCT) » PVR increase reported in 14 studies. Range of 0 – 75% with half reporting rates of 43% or higher » Self-catheterization rates (0 – 43%) reported in 20 studies; 6 studies with rates >20% » Increased PVRs and need for self-catheterization persist for 6 – 9 months in some patients » In one assessment, 54% of patients reported 1+ side-effect including dry mouth (19.6%), gross hematuria (17.9%), urinary retention (8.9%), eyelid weakness (8.9%), arm weakness (8.9%), UTI (7.1%), leg weakness (7.1%), dysphagia (5.4%), torso weakness (5.4%), impaired vision (5.4%). Urinary retention and UTI required further treatment	"In contrast to PTNS studies … SNS studies reported frequent adverse events …" » Pain at the stimulator site (3.3 – 19.8%) » Pain at the lead site (4.5 – 19.1%) » Lead migration (2.2 – 8.6%) » Infection/irritation (2.2 – 14.3% of patients) » Electric shock (5.5 – 10.2%) » Need for surgical revision (6.25 – 39.5%). In most studies it was >30% of patients » One study indicated that while 90% of patients reported satisfaction with SNS, 56% reported adverse events
Quality of Evidence	• ~20 studies • Predominantly observational designs • Varying patient inclusion criteria • Small sample sizes • Short follow-up durations for most studies	• ~40 studies • Durations were short in the best-designed studies (ranging from 4 – 12 weeks for the RCTs) • Varying doses and injection sites • Varying adverse event reporting	• ~30 studies • Predominantly observational designs • Small sample sizes • Limited number of unique patient groups (multiple reports on the same patient groups) • Limited information regarding the protocols used by patients to maintain symptom control

Remarkable Results. Reduced Risk.

URGENT PC NEUROMODULATION SYSTEM

- Urgent PC is FDA-cleared to provide percutaneous tibial nerve stimulation (PTNS)
- PTNS data cited in the AUA/SUFU OAB Guideline is predominantly from clinical studies performed with Urgent PC and its predicate device
- Up to 80% of patients respond; consistent results in 50 clinical studies[3-5]
- Significant improvements in urgency, incontinence episodes, frequency, nighttime voids and QoL[4,5]
- Office treatment with no recovery time and virtually no lingering side-effects
- 12 weekly, 30-minute sessions to gain maximum results; improvements sustained with a treatment about once a month[4,5]



1. American Urological Association. (2014). Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU Guideline Algorithm [chart]. Retrieved May 19, 2014 from the American Urological Association website: http://www.auanet.org/content/media/OAB_algorithm.pdf
2. American Urological Association. (2014). Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU Guideline. Retrieved May 19, 2014 from the American Urological Association website: http://www.auanet.org/content/media/OAB_guideline.pdf
3. Data on file.
4. MacDiarmid, S.A., Peters, K.M., Shobeiri, S.A., Wooldridge, L.S., Rovner, E.S., Leong, F.C., et al. (2010). Long-term durability of percutaneous tibial nerve stimulation for the treatment of overactive bladder. *J Urol, 183*(1), 234-40.
5. Peters, K., Carrico, D., Wooldridge, L., Miller, C., & MacDiarmid, S. (2013). Percutaneous tibial nerve stimulation for the long-term treatment of overactive bladder: 3-year results of the STEP Study. *J Urol, 189*(6), 2194-2201.

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