Treatment of OAB and the Managed Care Professional: Balancing the Double-Edged Sword

Roger Dmochowski, MD, MMHC, FACS
Professor of Urology, Surgery, and Gynecology
Vanderbilt University Medical Center
Nashville, TN

David Staskin, MD
Associate Professor, Urology
Tufts University School of Medicine
Boston, MA

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Disclosures

- Roger Dmochowski, MD, MMHC, FACS
  - Consulting Fees: Urovant Sciences
- David Staskin, MD
  - Consulting Fees: Astellas Pharma, Inc., Urovant Sciences
  - Research: Astellas Pharma, Inc., Urovant Sciences

Learning Objectives

1. Identify strategies for screening patients who are likely to have overactive bladder (OAB)
2. Discuss tactics for communicating with older patients about symptoms of OAB
3. Incorporate patient preferences into the treatment of OAB
4. Compare the risks and benefits of treatment options for OAB

Defining Overactive Bladder (OAB)

OAB

- ***Urinary urgency***, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence (UUI), in the absence of urinary tract infection or other obvious pathology

Haylen BT, et al. *Neurourol Urodyn*. 2010;29(1):4-20.

Defining Overactive Bladder (OAB)

OAB

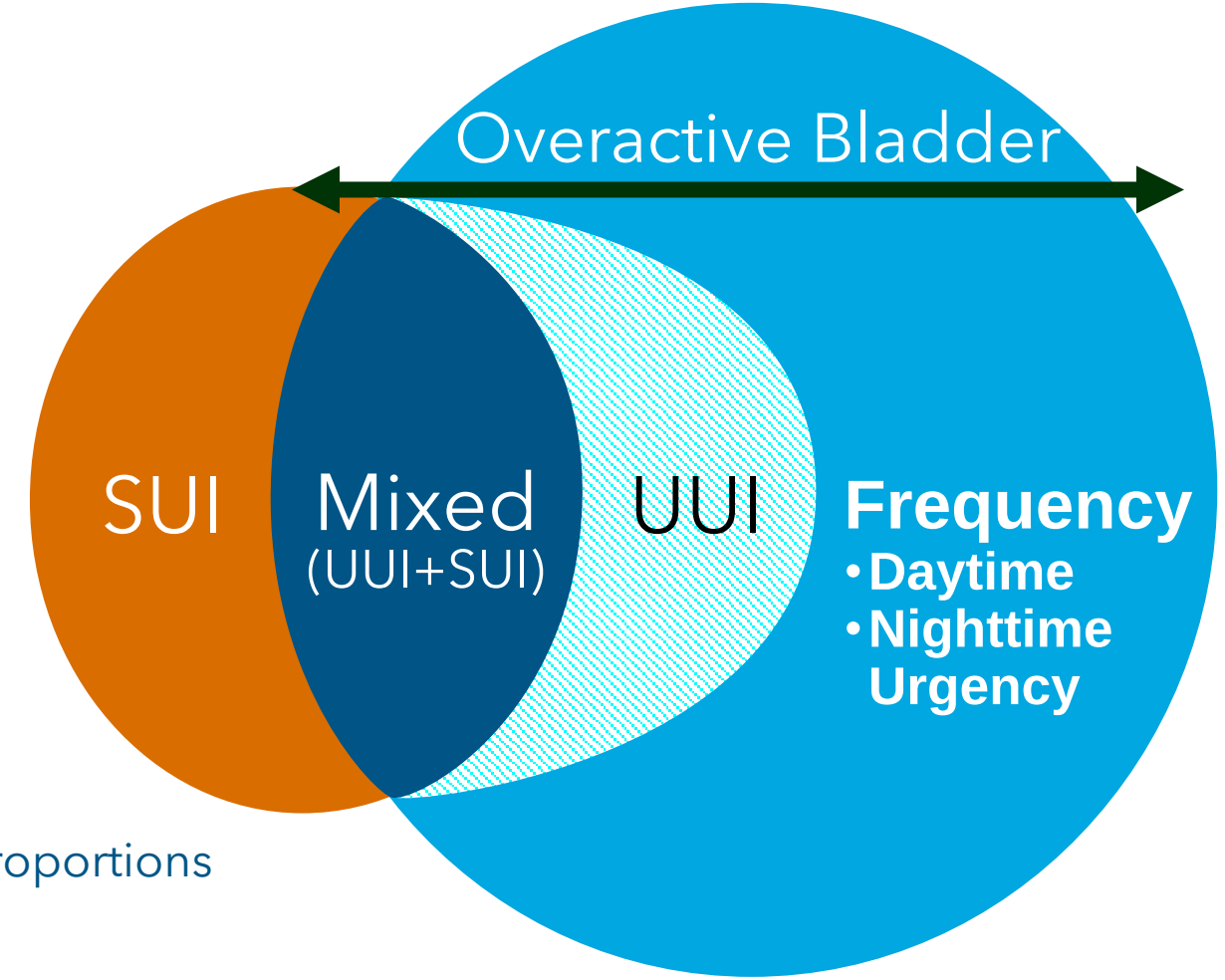
- ***Urinary urgency***, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence (UUI), in the absence of urinary tract infection or other obvious pathology

Urgency

- Sudden, compelling desire to pass urine which is difficult to defer

Haylen BT, et al. *Neurourol Urodyn*. 2010;29(1):4-20.

Spectrum of Overactive Bladder



Varying proportions

OAB Is Bothersome: Data from EpiLUTS

Lower Urinary Tract Symptoms*	Women	Men
Prevalence "at least sometimes," %	43.1	27.2
Prevalence "at least often," %	32.6	15.8
Bothersome symptoms, %	Sometimes 67.6 (at least somewhat) 38.9 (quite a bit) Often 73.0 (at least somewhat) 47.1 (quite a bit)	Sometimes 60.0 (at least somewhat) 27.8 (quite a bit) Often 67.8 (at least somewhat) 38.2 (quite a bit)

*Urgency and urgency urinary incontinence

Coyne KS, et al. *Urology*. 2011;77(5):1081-1087.

OAB Affects 1 Out of 7 Women and Men in the US

Prevalence, %	Black	Hispanic	Asian	White
Women	45.9*	42.0	26.6	43.4
Men	33.3	28.0	27.0	26.3

*Report the highest prevalence of urge-UI

Reynolds WS, et al. *Curr Bladder Dysfunct Rep*. 2016;11(1):8-13.

Common Risk Factors for OAB

- **Most common cause is idiopathic**
- Diseases that affect the brain or spinal cord
- Central nervous system disorders
- Older age (risk increases with age)
- Senile or presenile dementias
- Alzheimer's disease
- Cognitive dysfunction

Health Burden of OAB

- Decreased QoL
  - Socialization
  - Physical activity
  - Weight gain
  - Self-esteem
  - Sexuality
  - Sleep
- Economics

Reynolds WS, et al. *Curr Bladder Dysfunct Rep*. 2016;11(1):8-13.

Typical Patient Profile

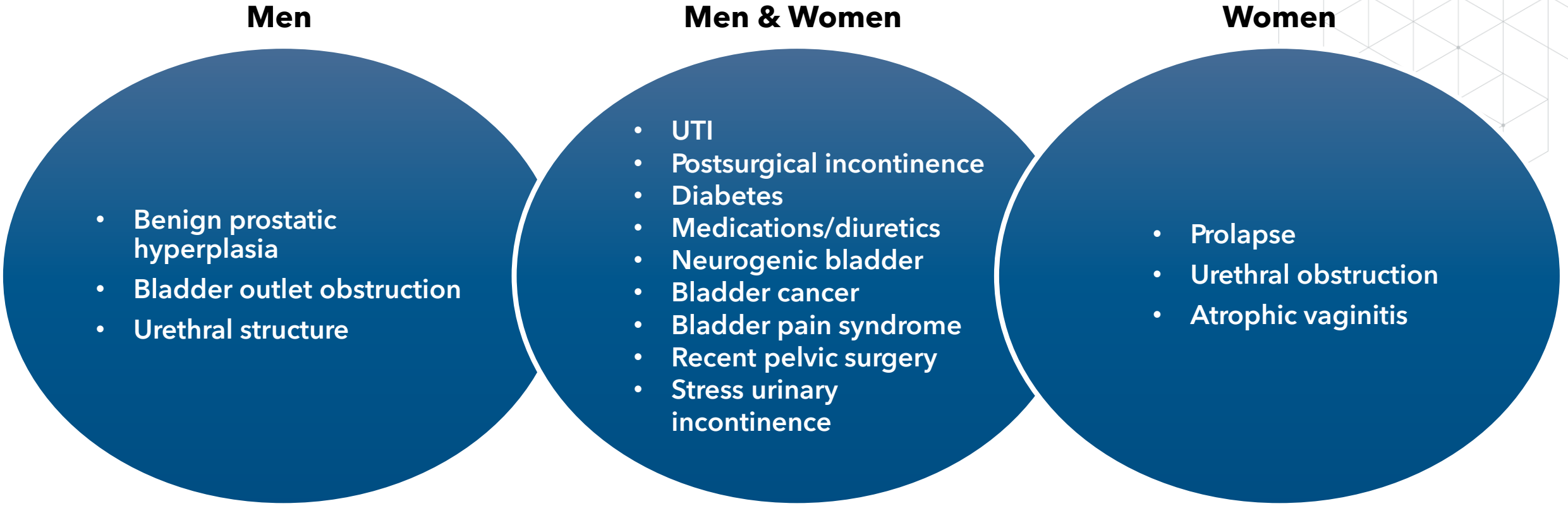
- Chief complaint
- Previous treatment for OAB
- Medical history
- Current medications
- Workup

Comprehensive Clinical Workup

- Detailed medical history
- Assessment of urinary symptoms & duration
  - Including storage and voiding symptoms
- Assessment of QoL and desire for treatment
- Physical examination
  - Abdominal, pelvic, and perineal examination
  - Brief neurologic examination
  - Cough test to demonstrate stress incontinence, if necessary
- Assessment of voluntary pelvic floor muscle contraction

Nitti V. *Can Urol Assoc J*. 2011;5(5 Suppl 2):S137-S138.

Differential Diagnosis of OAB



Gormley EA, et al. *J Urol*. 2015;193(5):1572-1580.

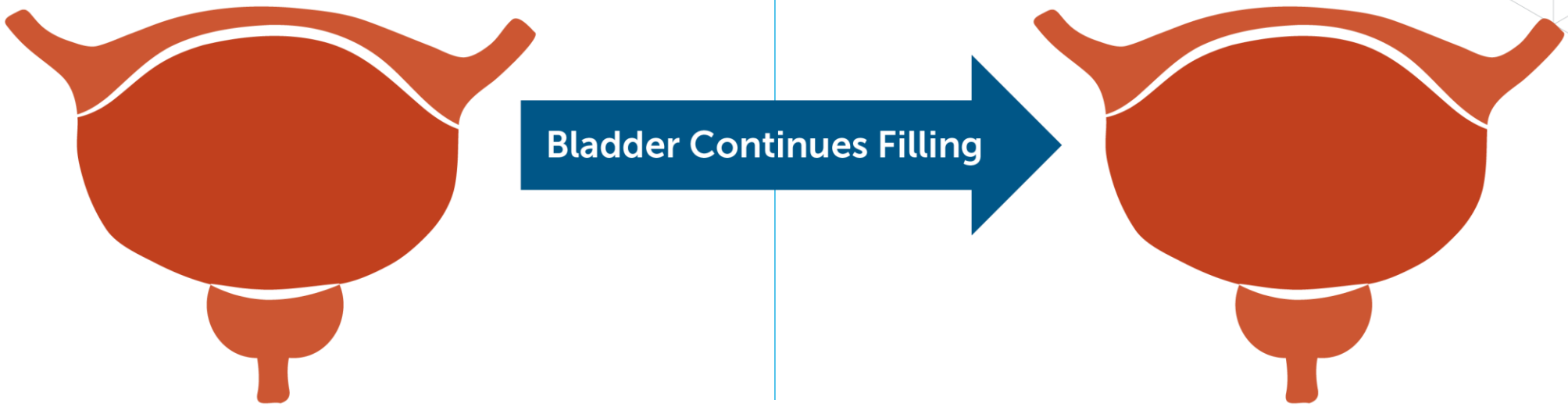
Pathophysiology of OAB: Normal Bladder Function

Filling/Storage Phase

- Urethra contracted
- Low bladder pressure
- Detrusor smooth muscle relaxed

Emptying Phase

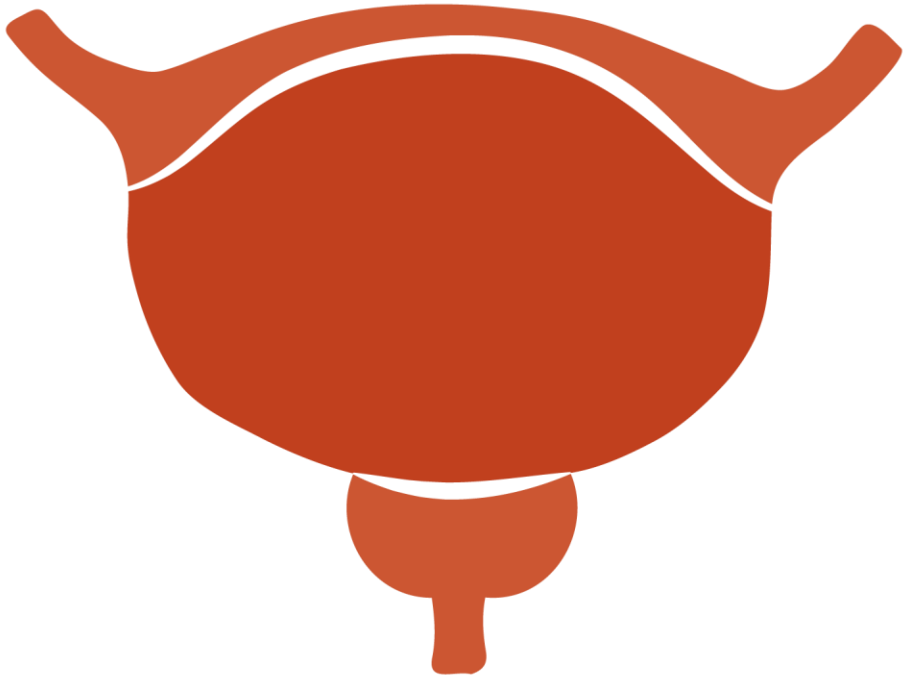
- Urethra relaxes
- Increased bladder pressure
- Detrusor smooth muscle contracts



Andersson KE, et al. *Physiol Rev*. 2004;84(3):935-986.
Ouslander JG. *N Engl J Med*. 2004;350(8):786-799.

Sympathetic and Parasympathetic Nervous Systems

Sympathetic:
relaxes bladder

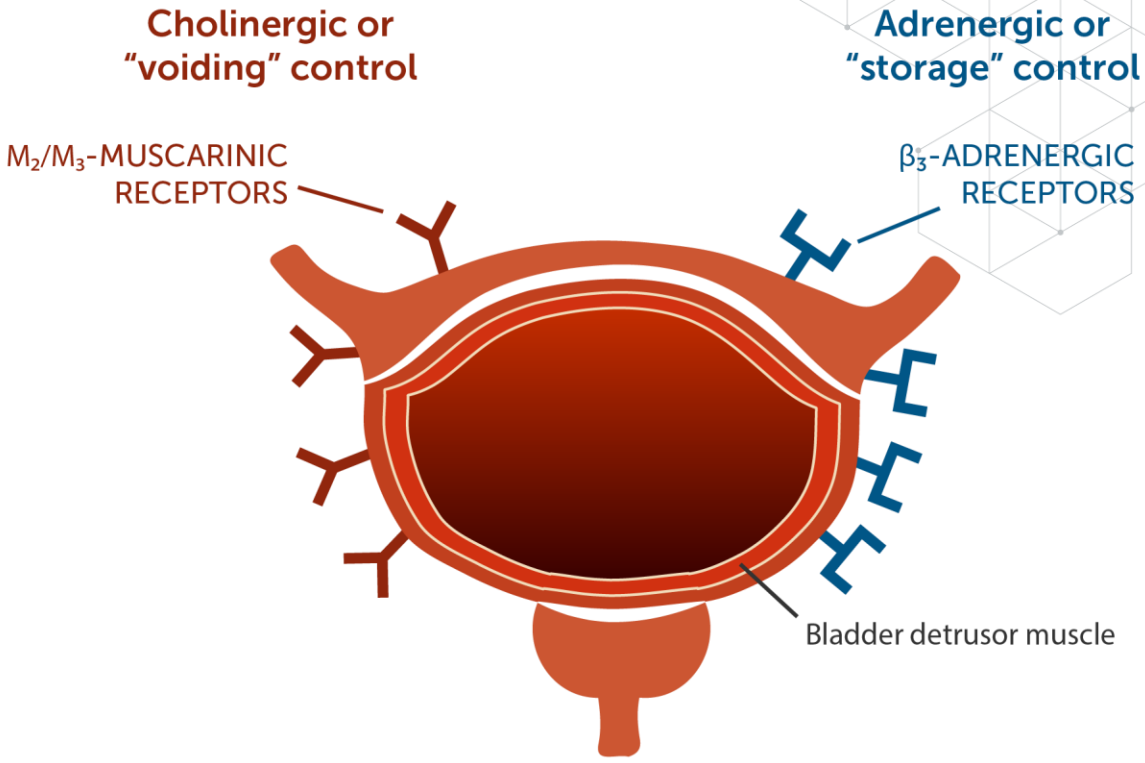


Parasympathetic:
contracts bladder

McCorry LK. *Am J Pharm Educ*. 2007;71(4):78.

2 Classes of Pharmacologic Therapy Are Approved to Treat OAB Symptoms

- B3-adrenergic receptor agonists
  - Activates the β3-adrenergic receptors in the bladder
  - Relaxes the detrusor smooth muscle, which increases bladder capacity
- Anti-muscarinics
  - Inhibit binding of acetylcholine to muscarinic receptors in the bladder
  - Leads to suppression of detrusor muscle contractions, which delays the initial desire to void

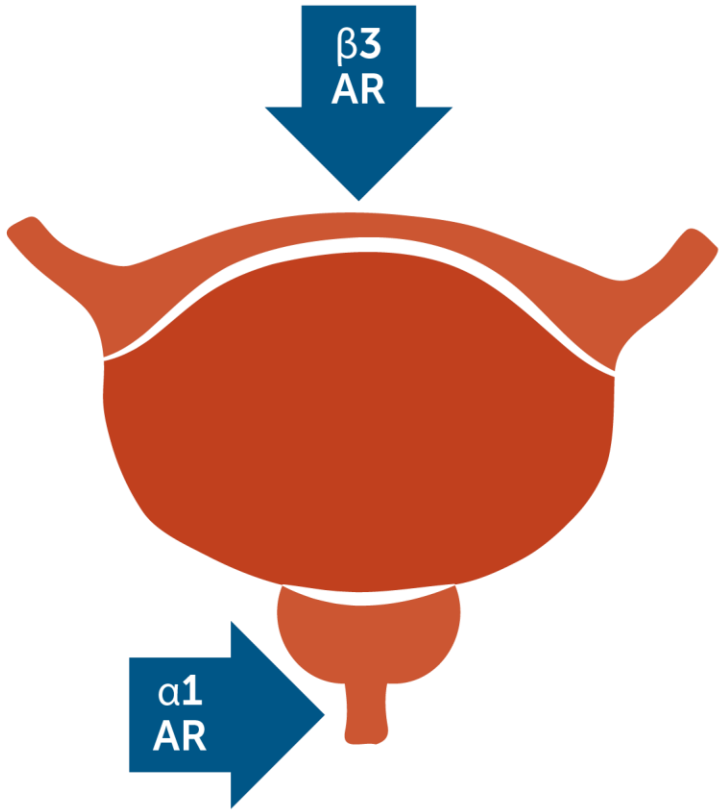


Predominant Muscarinic Receptors in the Human Body

- Brain: M1
  - Cross-reactivity with the brain
- Eye: M1, M3, M5
  - Blurry vision
- Salivary glands: M1/M3
  - Dry mouth
- Heart: M2/M3
  - Effects on pulse rate
- GI tract: M2/M3
  - Effects on constipation
- **Bladder: M2/M3**

Abrams P, et al. *Br J Pharmacol*. 2006;148(5):565-578.

Sympathetic Regulation of Bladder Storage

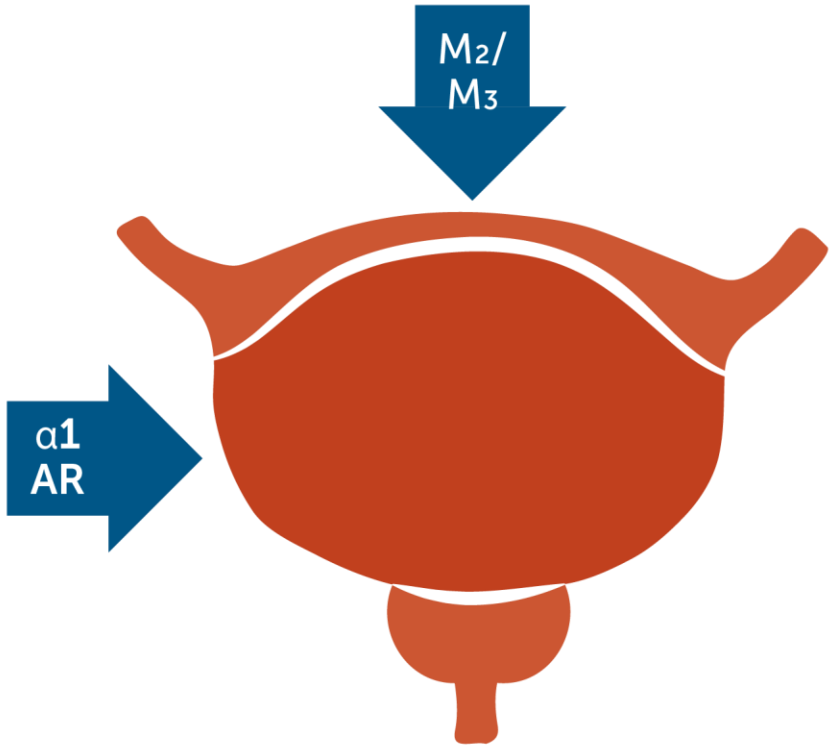


- SNS releases NE and activates adrenergic receptors on the bladder
- NE binding to β3 ARs relaxes detrusor muscle
- NE plays dual role in regulating bladder storage
- NE binding to α1 ARs contracts internal sphincter muscle

AR, adrenoceptor; NE, norepinephrine; SNS, sympathetic nervous system.

Fowler CJ, et al. *Nat Rev Neurosci*. 2008;9(6):453-466. Ouslander JG. *N Engl J Med*. 2004;350(8):786-799. Takeda M, et al. *J Pharmacol Sci*. 2010;112(2):121-127.

Parasympathetic Regulation of Bladder Storage



- PNS releases ACh and activates muscarinic receptors on the bladder
- ACh binding to muscarinic receptors contracts detrusor muscle
- NE plays dual role in regulating bladder storage
- NE binding to α1 ARs contracts internal sphincter muscle

ACh, acetylcholine; AR, adrenoceptor; NE, norepinephrine; PNS, parasympathetic nervous system.

Abrams P, et al. *Br J Pharmacol*. 2006;148(5):565-578. Clemens JQ. *Urol Clin North Am*. 2010;37(4):487-494. Andersson KE. *Pharmacol Rev*. 1993;45(3):253-308.

Screening Begins With a Discussion

SYMPTOM QUESTIONS	Not at all	Occasionally	About once a day	About three times a day	About half the time	Almost always	SCORE
1. Urgency – How often do you have a strong, sudden urge to urinate that makes you fear you will leak urine if you can't get to a bathroom immediately?	0*	1	2	3	4	5	
2. Urgency Incontinence – How often do you leak urine after feeling a strong urge to go? (whether you wear pads/protection or not)	0	1	2	3	4	5	
	None	Drops	1 Tea-spoon	1 Table-spoon	¼ cup	Entire bladder	
3. Incontinence – How much urine do you think usually leaks? (whether you wear pads/protection or not)	0	1	2	3	4	5	
	1-6 times	7-8 times	9-10 times	11-12 times	13-14 times	15 or more times	
4. Frequency – How often do you urinate during the day?	0	1	2	3	4	5	
	None	1 time	2 times	3 times	4 times	5 times or more	
5. Waking to urinate – How many times do you usually get up at night to urinate, from when you went to bed until you get up in the morning?	0	1	2	3	4	5	

TOTAL SYMPTOM SCORE Add score from questions 1+2+3+4+5 =

**If you score 0 on question 1, you probably don't have OAB.*

0 = no symptoms
5 = most severe symptoms

QUALITY OF LIFE QUESTIONS How much does this bother you:	I am not bothered at all					I am bothered a great deal
1b. Urgency – a strong, sudden urge to urinate that makes you fear you will leak urine if you can't get to a bathroom immediately?	0	1	2	3	4	5
2b. Urgency Incontinence – leaking after feeling an urge to go?	0	1	2	3	4	5
3b. Frequency – urinating frequently	0	1	2	3	4	5
4b. Waking from sleep to urinate?	0	1	2	3	4	5
	I would not be bothered at all					I would be bothered a great deal
5b. Overall satisfaction – If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?	0	1	2	3	4	5

6b. How have your symptoms changed your life? – How have your symptoms (urgency, frequency, urine leakage, and waking at night) changed your life? Are your symptoms:

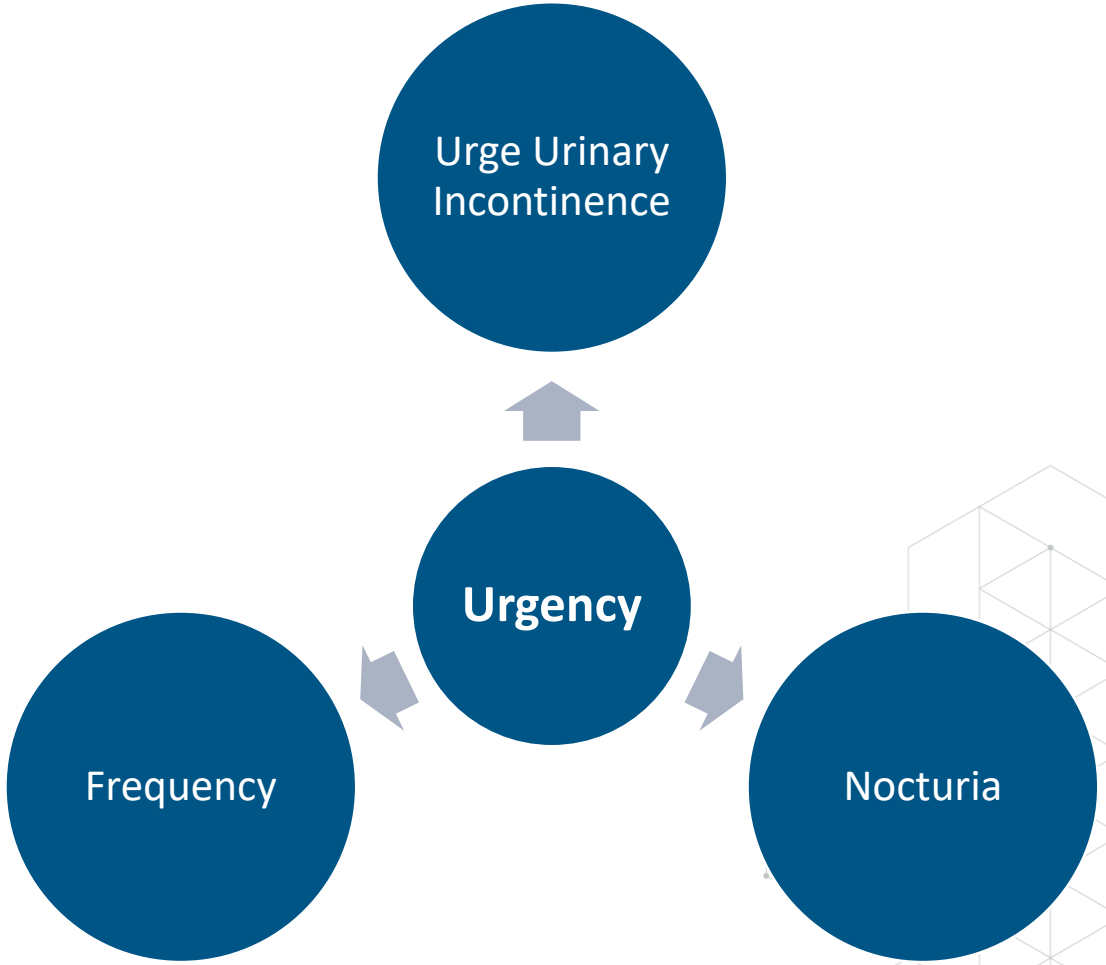
(Please check all that apply)

- ○ Keeping you from getting a good night's sleep?
- ○ Causing you to stay home more than you would like?
- ○ Keeping you from social activities or entertainment?
- ○ Causing you to exercise less or limit your physical activity?
- ○ Causing problems with friends or loved ones?
- ○ Keeping you from traveling, taking trips, or using public transit?
- ○ Making you plan trips around your knowledge of public restroom location?
- ○ Causing problems at work?
- ○ Other ways your symptoms have changed your life:

Urology Care Foundation.
https://www.urologyhealth.org/educational-resources/overactive-bladder-assessment-tool

Screening for OAB: Urgency – A Core Symptom

- Urinary urgency, usually accompanied by increased daytime frequency and/or nocturia, with urinary incontinence (OAB wet) or without (OAB dry) in the absence of UTI or other detectable disease



Yamaguchi O, et al. *Neurourol Urodyn*. 2007;26(6):752-756. Fowler CJ, et al. *Nat Rev Neurosci*. 2008;9(6):453-466. Abrams P, et al. *Br J Pharmacol*. 2006;148(5):565-578.

OAB Assessment Tool: Frequency of Symptoms

1. **Urgency** – How often do you have a strong, sudden urge to urinate that makes you fear you will leak urine if you can't get to a bathroom immediately?
2. **Urgency incontinence** – How often do you leak urine after feeling a strong urge to go? (whether you wear pads/protection or not)
3. **Incontinence** – How much urine do you think usually leaks? (whether you wear pads/protection or not)
4. **Frequency** – How often do you urinate during the day?
5. **Waking to urinate** – How many times do you usually get up at night to urinate, from when you went to bed until you get up in the morning?

Urology Care Foundation. https://www.urologyhealth.org/educational-resources/overactive-bladder-assessment-tool

Screening for OAB: Urgency Is a Core Symptom

Symptom	Definition
Urgency	Sudden, compelling desire to urinate
Nocturia	Interruptions of sleep ≥1 time due to need to void
Frequency	≥8 micturitions (variable) during waking hours
UUI	UUI: involuntary urine leakage with sudden compelling desire to void (OAB wet)

Yamaguchi O, et al. *Neurourol Urodyn*. 2007;26(6):752-756. Fowler CJ, et al. *Nat Rev Neurosci*. 2008;9(6):453-466. Abrams P, et al. *Br J Pharmacol*. 2006;148(5):565-578.

AUA/SUFU Guidelines

Roger Dmochowski, MD

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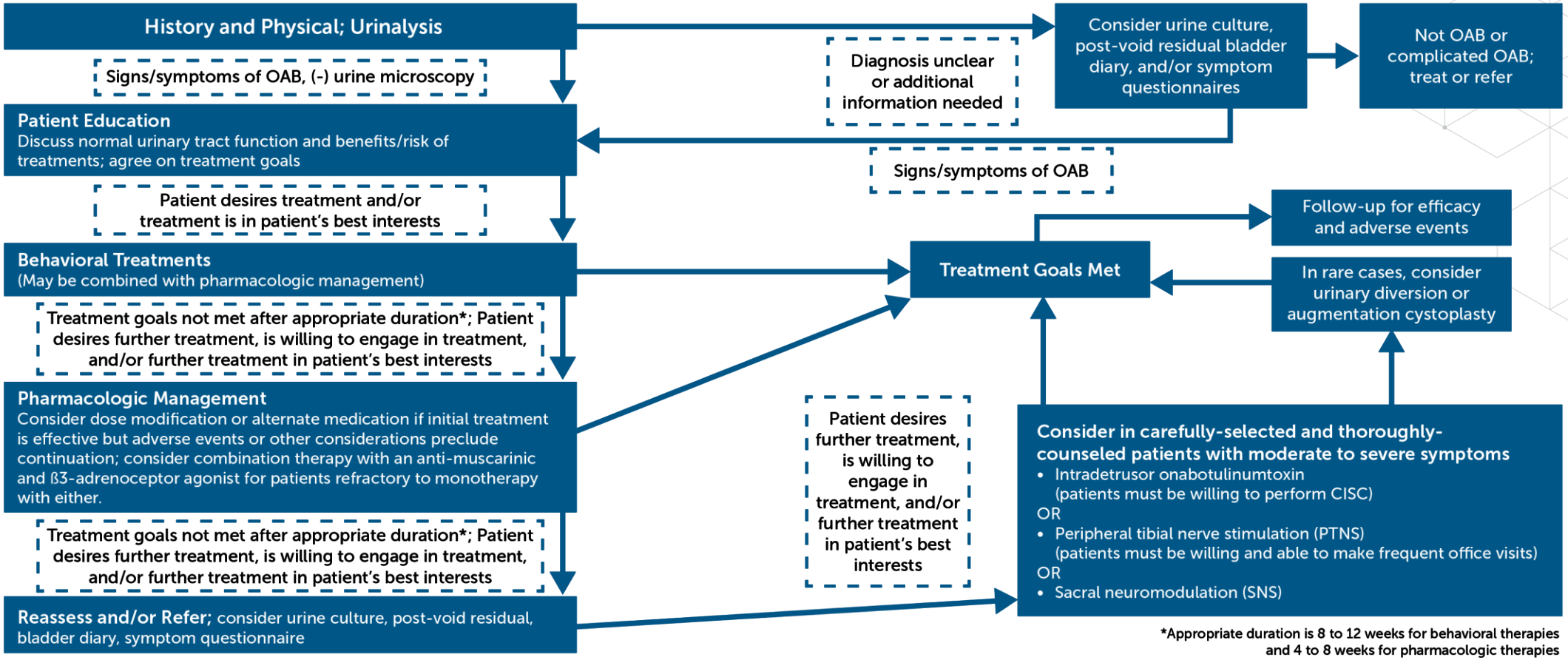
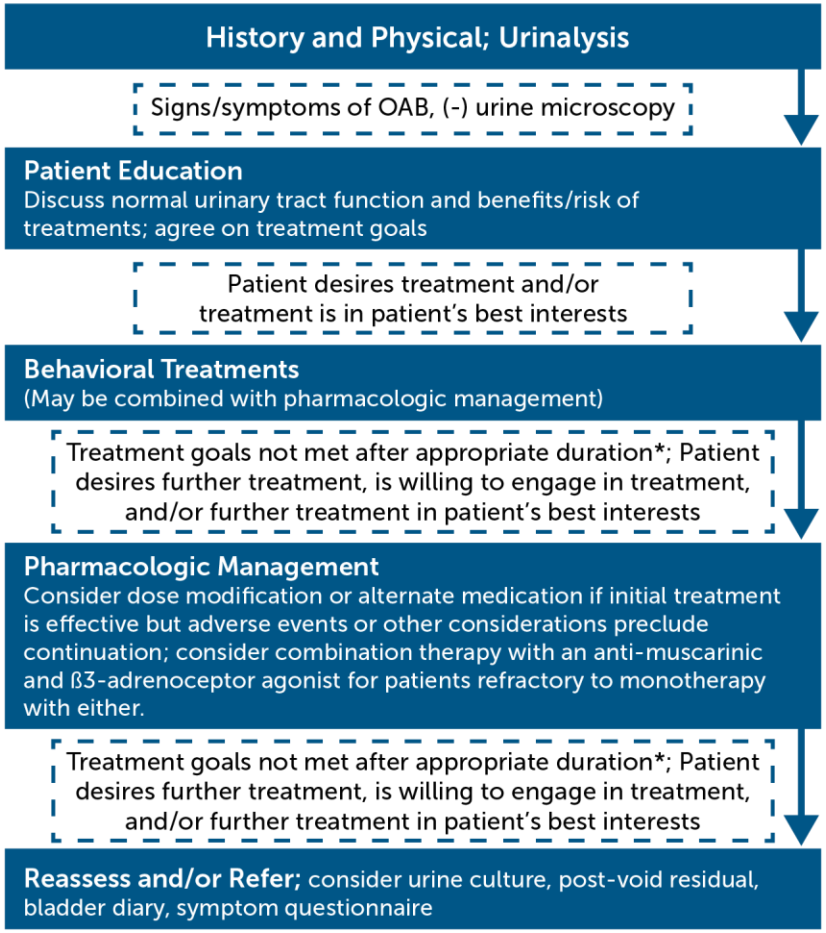
Diagnosis & Treatment Algorithm: AUA/SUFU Guideline on Non-Neurogenic Overactive Bladder in Adults



The complete OAB Guideline is available at AUAnet.org/Guidelines.
This clinical framework does not require that every patient go through each line of treatment in order as there are many factors to consider when identifying the best treatment for a particular patient.

Lightner DJ, et al. *J Urol.* 2019;202(3):558-563.

Diagnosis & Treatment Algorithm: AUA/SUFU Guideline on Non-Neurogenic Overactive Bladder in Adults



*Appropriate duration is 8 to 12 weeks for behavioral therapies and 4 to 8 weeks for pharmacologic therapies

Lightner DJ, et al. *J Urol*. 2019;202(3):558-563.

First-Line Treatments: Behavioral Therapies

- Clinicians should offer ***behavioral therapies*** (eg, bladder training, bladder control strategies, pelvic floor muscle training, fluid management) as first-line therapy to all patients with OAB
- ***Behavioral therapies*** may be combined with pharmacologic management

Lightner DJ, et al. *J Urol*. 2019;202(3):558-563.
Gormley EA, et al. *J Urol*. 2012;188(6 Suppl):2455-2463.

Second-Line Treatments: Pharmacologic Management

- Clinicians should offer ***oral anti-muscarinics*** or ***oral β_3-adrenoceptor agonists*** as second-line therapy
- If an immediate-release (IR) and an extended-release (ER) formulation are available, then ER formulations should be preferentially prescribed over IR formulations because of lower rates of dry mouth
- Transdermal oxybutynin (patch or gel) may be offered
- If a patient experiences inadequate symptom control and/or unacceptable adverse drug events with 1 anti-muscarinic medication, then a dose modification or a different anti-muscarinic medication or a β_3-adrenoceptor agonist may be tried

Lightner DJ, et al. *J Urol.* 2019;202(3):558-563.
Gormley EA, et al. *J Urol.* 2012;188(6 Suppl):2455-2463.

Second-Line Treatments: Pharmacologic Management

- Clinicians may consider ***combination therapy*** with an anti-muscarinic and β_3-adrenoceptor agonist for patients refractory to monotherapy with either anti-muscarinics or β_3-adrenoceptor agonists
- Clinicians should not use anti-muscarinics in patients with narrow-angle glaucoma unless approved by the treating ophthalmologist; anti-muscarinics should be used with extreme caution in patients with impaired gastric emptying or a history of urinary retention
- Clinicians should manage constipation and dry mouth before abandoning effective anti-muscarinic therapy; management may include bowel or fluid management, dose modification, or alternative anti-muscarinics.

Lightner DJ, et al. *J Urol.* 2019;202(3):558-563.
Gormley EA, et al. *J Urol.* 2012;188(6 Suppl):2455-2463.

Second-Line Treatments: Pharmacologic Management

- Clinicians should use caution in prescribing anti-muscarinics in patients who are using other medications with anti-cholinergic properties
- Clinicians should use caution in prescribing anti-muscarinics or β_3-adrenoceptor agonists in the frail OAB patient
- Patients who are refractory to behavioral and pharmacologic therapy should be evaluated by an appropriate specialist if they desire additional therapy

Lightner DJ, et al. *J Urol.* 2019;202(3):558-563.
Gormley EA, et al. *J Urol.* 2012;188(6 Suppl):2455-2463.

Third-Line Treatments: PTNS and Neuromodulation

- 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
- Clinicians may offer ***peripheral tibial nerve stimulation*** (PTNS) as third-line treatment in a carefully selected patient population

Lightner DJ, et al. *J Urol*. 2019;202(3):558-563.
Gormley EA, et al. *J Urol*. 2012;188(6 Suppl):2455-2463.

Third-Line Treatments: PTNS and Neuromodulation

- 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

Lightner DJ, et al. *J Urol*. 2019;202(3):558-563.
Gormley EA, et al. *J Urol*. 2012;188(6 Suppl):2455-2463.

Third-Line Treatments: PTNS and Neuromodulation

- 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

Lightner DJ, et al. *J Urol*. 2019;202(3):558-563.
Gormley EA, et al. *J Urol*. 2012;188(6 Suppl):2455-2463.

Fourth-Line Treatments: Augmentation Cystoplasty and Urinary Diversion

- In rare cases, ***augmentation cystoplasty or urinary diversion*** may be considered for patients with severe, refractory, complicated OAB

Lightner DJ, et al. *J Urol*. 2019;202(3):558-563.
Gormley EA, et al. *J Urol*. 2012;188(6 Suppl):2455-2463.

Additional Treatments?

- Indwelling catheters (including transurethral, suprapubic, etc.) are not recommended as a management strategy for OAB because of the adverse risk/benefit balance except as a last resort in selected patients

Lightner DJ, et al. *J Urol*. 2019;202(3):558-563.
Gormley EA, et al. *J Urol*. 2012;188(6 Suppl):2455-2463.

Pharmacologic Agents

David Staskin, MD

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EMPOWUR Study Design and Endpoints

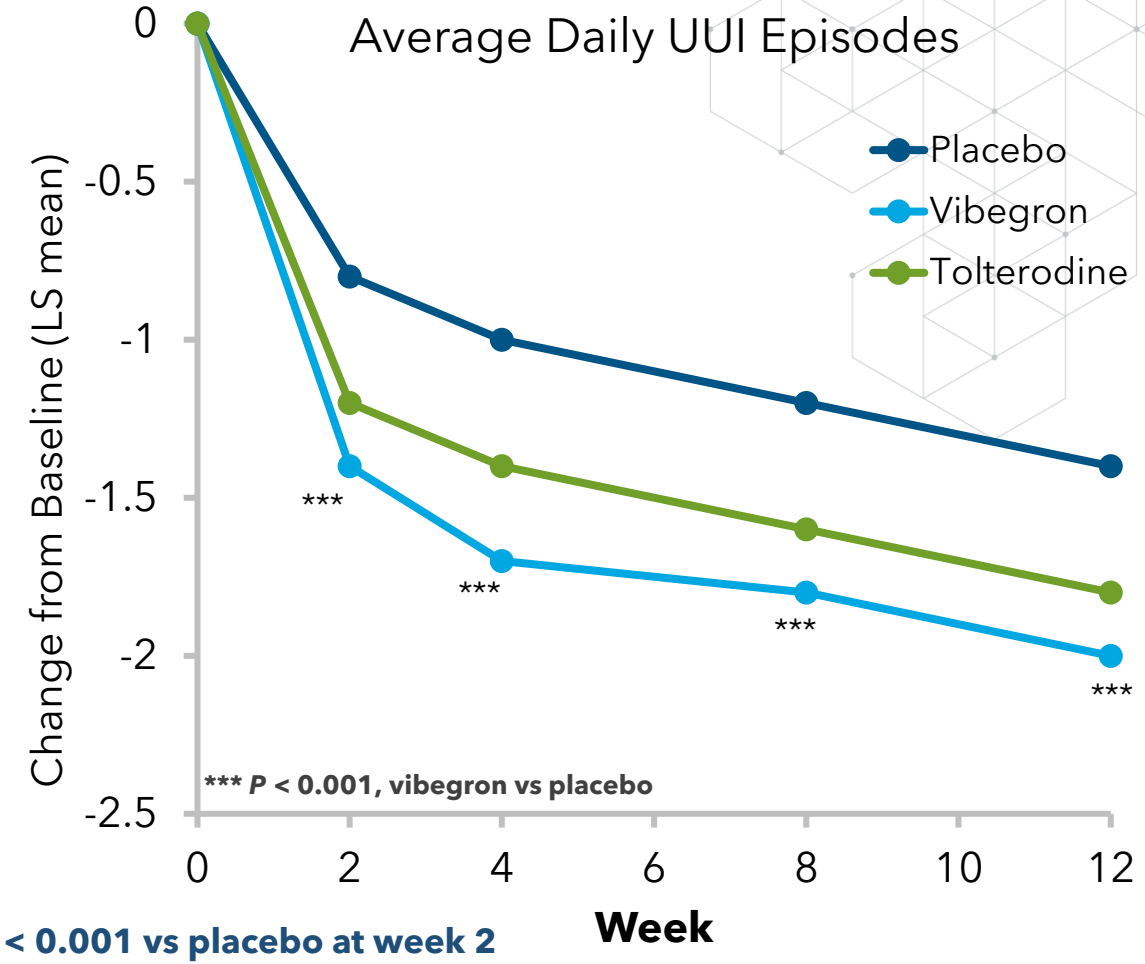
- 12-week treatment period with a 4-week safety follow-up
- Randomized 5:5:4 to 75 mg vibegron, placebo, and tolterodine ER 4 mg once daily
  - Primary statistical comparison (powered) – vibegron vs placebo
  - Tolterodine – active control; statistical testing vs placebo (only) per protocol
- **Co-primary endpoints at week 12**
  - Change in the average number of daily urge urinary incontinence (UUI) episodes in patients with ≥1 UUI episode per day
  - Change in average number of daily micturitions
- **Key secondary endpoints at week 12**
  - Change in average number of daily urgency episodes
  - Change in volume voided per micturition

Vibegron Significantly Reduces Daily UUI Episodes at Week 12

Daily Urge Urinary Incontinence Episodes

	Placebo	Vibegron	Tolterodine
Baseline Mean (n)	3.49 (405)	**3.43 (403)**	3.42 (319)
LS Mean CFB† at 12 Weeks (n)	-1.4 (372)	**-2.0 (383)**	-1.8 (286)
LS Mean Difference vs Placebo (95% CI) *P* value	–	**-0.6 (-0.9, -0.3) *P* < 0.0001**	-0.4 (-0.7, -0.1) *P* = 0.0123††

† CFB, change from baseline.
†† Tolterodine *P* value vs placebo, per protocol.
Table 14.2.2.1.2 Full Analysis Set for Incontinence



Rapid response achieved with vibegron; *P* < 0.001 vs placebo at week 2

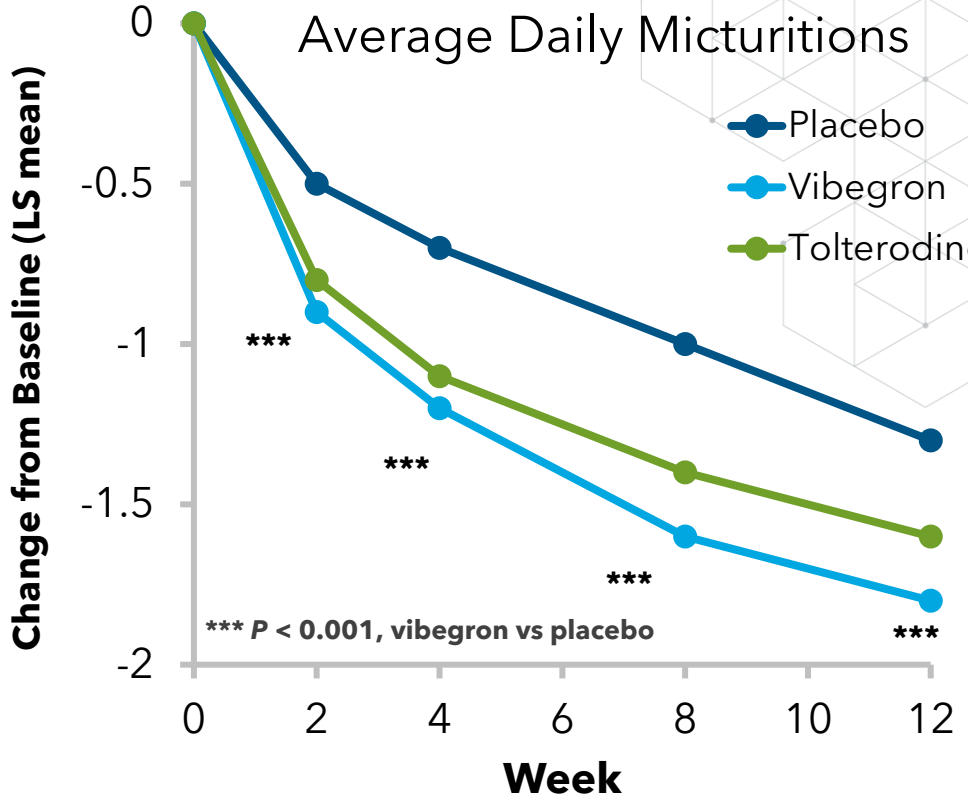
Staskin D, et al. *J Urol*. 2020;204(2):316-324.

Vibegron Significantly Reduces Daily Micturitions at Week 12

Daily Micturitions

	Placebo	Vibegron	Tolterodine
Baseline Mean (n)	11.75 (520)	**11.31 (526)**	11.48 (417)
LS Mean CFB† at 12 Weeks (n)	-1.3 (475)	**-1.8 (492)**	-1.6 (378)
LS Mean Difference vs Placebo (95% CI) *P* value	–	**-0.5 (-0.8, -0.2) *P* < 0.001**	-0.3 (-0.6, 0.1) *P* = 0.0988††

† CFB, change from baseline.
†† Tolterodine *P* value vs placebo, per protocol.
Table 14.2.2.1.2 Full Analysis Set for Incontinence



vibegron; *P* < 0.001 vs placebo at week 2

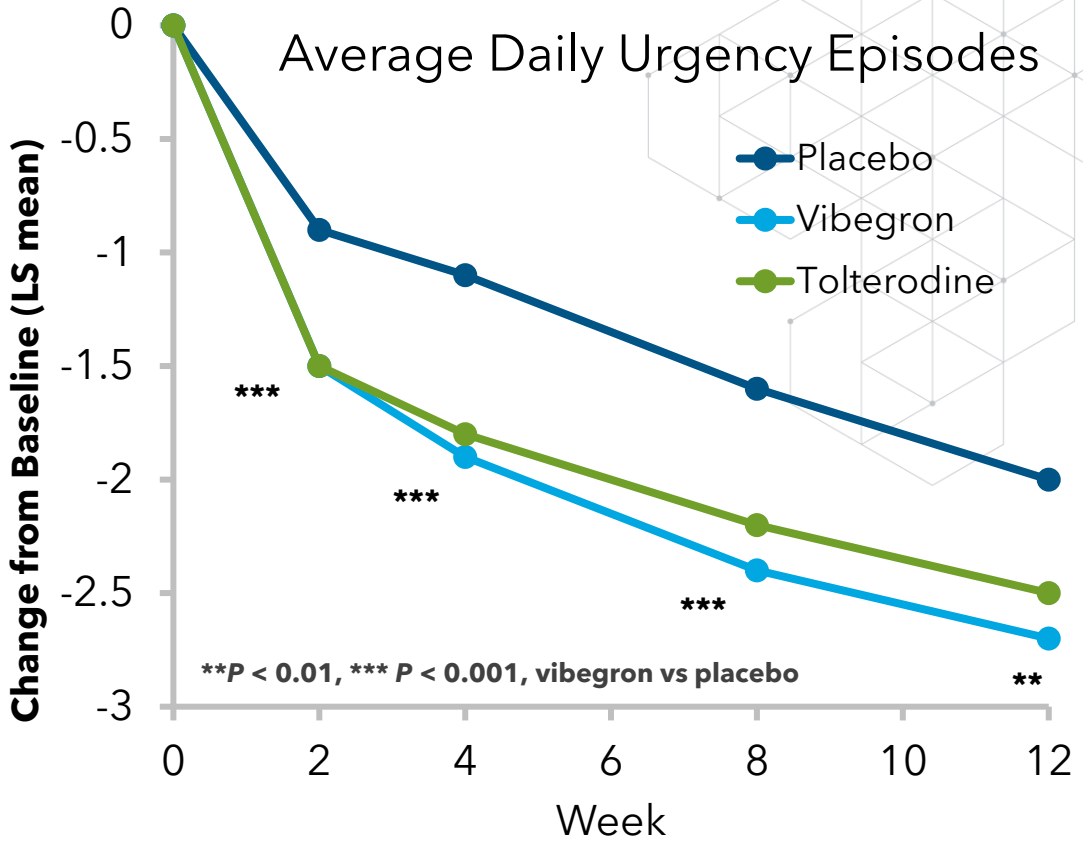
Staskin D, et al. *J Urol*. 2020;204(2):316-324.

Vibegron Significantly Reduces Daily Urgency Episodes at Week 12

Daily Urgency Episodes

	Placebo	Vibegron	Tolterodine
Baseline Mean (n)	8.13 (520)	**8.11 (526)**	7.92 (417)
LS Mean CFB† at 12 Weeks (n)	-2.0 (475)	**-2.7 (492)**	-2.5 (378)
LS Mean Difference vs Placebo (95% CI) *P* value	–	**-0.7 (-1.1, -0.2) *P* = 0.0020**	-0.4 (-0.9, 0.0) *P* = 0.0648††

† CFB, change from baseline.
†† Tolterodine *P* value vs placebo, per protocol.
Table 14.2.2.1.2 Full Analysis Set for Incontinence



Rapid response achieved with vibegron; *P* < 0.001 vs placebo at week 2

Staskin D, et al. *J Urol*. 2020;204(2):316-324.

Vibegron Significantly Increases Volume Voided Per Micturition at Week 12

Volume Voided (per micturition)

	Placebo	Vibegron	Tolterodine
Baseline Mean (n)	148.3 (514)	**155.4 (524)**	147.0 (415)
LS Mean CFB† at 12 Weeks (n)	2.2 (478)	**23.5 (490)**	15.5 (375)
LS Mean Difference vs Placebo (95% CI) *P* Value	-----	**21.2 (14.3, 28.1) <0.0001**	13.3 (5.9, 20.7) <0.001††

† CFB, change from baseline.
†† Tolterodine *P* value vs placebo, per protocol.
Table 14.2.9.1.2 Full Analysis Set

Rapid response achieved with vibegron; *P* < 0.001 vs placebo at week 2

Staskin D, et al. *J Urol*. 2020;204(2):316-324.

Vibegron Efficacy in Key Subpopulations at Week 12

Subpopulation	Placebo	Vibegron	Tolterodine
Age ≥ 65 years (micturitions)	-1.27 (2.67) n = 204	**-2.10** (2.83) n = 228	-1.48 (2.15) n = 151
Age ≥ 65 years (UUI episodes)	-1.20 (2.70) n = 158	**-1.94** (2.50) n = 183	-1.80 (2.41) n = 116
Prior anticholinergic use (micturitions)	-1.25 (2.33) n = 79	**-1.97** (2.40) n = 74	-1.52 (1.88) n = 48
Prior anticholinergic use (UUI episodes)	-0.83 (2.18) n = 68	**-1.46** (2.16) n = 64	-0.98 (1.80) n = 39
Prior mirabegron use (micturitions)	0.03 (2.22) n = 25	**-2.83** (3.83) n = 18	-1.30 (1.99) n = 31
Prior mirabegron use (UUI episodes)	-0.31 (1.62) n = 21	**-1.64** (2.59) n = 14	-0.65 (1.42) n = 18

Data presented as mean (SD) change from baseline to week 12

Table 14.2.1.1.9 Full Analysis Set; Table 14.2.2.1.9 Full Analysis Set for Incontinence

Staskin D, et al. *J Urol*. 2020;204(2):316-324.

Vibegron Demonstrated a Favorable Safety and Tolerability Profile

Safety Population, n (%)

	Placebo (N = 540)	Vibegron (N = 545)	Tolterodine (N = 430)
Patients with ≥1 treatment-emergent serious AE	6 (1.1)	8 (1.5)	10 (2.3)
Discontinued due to AEs, n (%)	6 (1.1)	8 (1.5)	13 (3.0)
Treatment-emergent AEs (Vibegron >2% and > Placebo)			
Headache	13 (2.4)	22 (4.0)	11 (2.6)
Nasopharyngitis	9 (1.7)	15 (2.8)	11 (2.6)
Diarrhea	6 (1.1)	12 (2.2)	9 (2.1)
Nausea	6 (1.1)	12 (2.2)	5 (1.2)
Selected AEs of Interest			
Hypertension	9 (1.7)	9 (1.7)	11 (2.6)
Blood pressure increased	5 (0.9)	4 (0.7)	8 (1.9)
Urinary tract infection	33 (6.1)	27 (5.0)	25 (5.8)
Urinary retention	2 (0.4)	3 (0.6)	3 (0.7)
Dry mouth	5 (0.9)	9 (1.7)	28 (6.5)

Table 14.3.1.1 Safety Set; Table 14.1.1.3 Randomized Set; Table 14.3.1.15 Safety Set; Table 14.3.1.14 Safety Set

Staskin D, et al. *J Urol*. 2020;204(2):316-324.

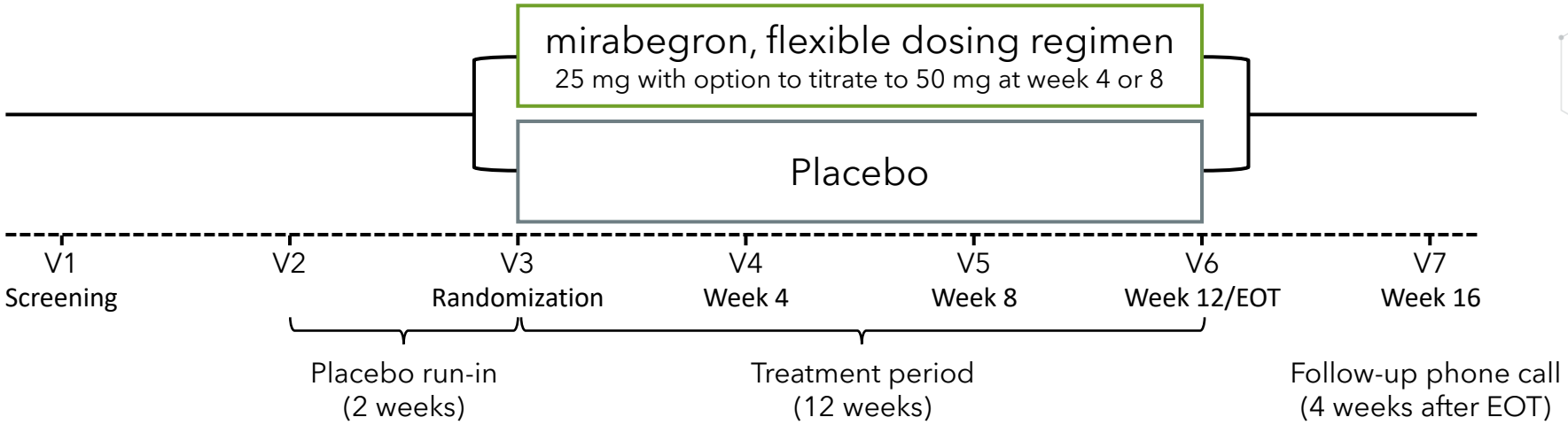
EMPOWUR Conclusions

- Vibegron 75 mg provided highly statistically significant improvement in OAB symptoms
  - Daily UUI episodes
  - Micturitions
  - Daily urgency episodes
  - Volume voided per micturition
- Rapid and significant onset of action by week 2, maintained through week 12
- Efficacy in key subpopulations at week 12
- Vibegron was well tolerated with a favorable safety profile
  - Few AEs were more common than placebo
  - Incidence of hypertension same as placebo

Staskin D, et al. *J Urol*. 2020;204(2):316-324.

PILLAR: Mirabegron Efficacy and Safety in Patients Aged ≥65 Years with OAB Symptoms

- Phase 4, double-blind, randomized, placebo-controlled study
- 3-day micturition diaries completed at baseline and before week 4, 8, and 12 (EOT)
- Patients with ≥1 incontinence episode, ≥3 urgency episodes (PPIUS grade 3 or 4), and ≥8 micturitions/24 h on average at baseline randomized 1:1 to mirabegron/placebo, stratified by age <75/≥75 years



Co-primary endpoints:
Change from baseline to EOT in mean number of micturitions and incontinence episodes/24 h for mirabegron total (25/50 mg) vs placebo

EOT, end-of-treatment; OAB, overactive bladder syndrome; PPIUS, Patient Perception of Intensity of Urgency Scale.

Herschorn S, et al. *Drugs Aging*. 2020;37(9):665-676.

Treatment-Emergent Adverse Events (SAF) Beta-3 Agonist in Patients >65 years old

	Placebo, N = 442	Beta3-agonist Total, N = 445
≥1 TEAE[a]	174 (39.4)	209 (47.0)
Drug-related TEAEs	57 (12.9)	84 (18.9)
Serious TEAEs	12 (2.7)	15 (3.4)
Serious drug-related TEAEs	2 (0.5)	0
TEAEs leading to discontinuation	14 (3.2)	14 (3.1)
Most frequent TEAEs[b]		
Urinary tract infection[c]	31 (7.0)	25 (5.6)
Headache	12 (2.7)	23 (5.2)
Diarrhea	6 (1.4)	13 (2.9)
Fatigue	14 (3.2)	10 (2.2)
Upper respiratory tract infection	10 (2.3)	10 (2.2)
Nausea	6 (1.4)	8 (1.8)
Dizziness	7 (1.6)	6 (1.3)
Nasopharyngitis	10 (2.3)	5 (1.1)

MedDRA version 20.1
a. Treatment-emergent adverse event (TEAE), an adverse event that started or worsened during the study period after first study medication dose.
b. Affecting ≥2% of any treatment group.
c. Escherichia urinary tract infection, streptococcal urinary tract infection, urinary tract infection, or urinary tract infection bacterial.

No significant change in Montreal Cognitive Assessment score during the study
Mean (SD) score change from baseline to EOT:
Placebo: 0.2 (2.3) Mirabegron Total: 0.1 (2.4)

Herschorn S, et al. *Drugs Aging*. 2020;37(9):665-676.

Case Presentation

Roger Dmochowski, MD

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Case Presentation

- CS is a 68-year-old G2 P1 female concerned about urinary symptoms
- Urgency incontinence for at least the last 2 years
- Daytime frequency 10, nocturia × 3
- Uses at least 2 pads per day
- Has tried fluid restriction and actively toilet maps
- PMHx: Mild CHF, depression
- Medications: Diuretic, antidepressant

Case Continued

- Family history: Mother had Alzheimer's disease (AD), father had ASCVD
- Social history: Banker, nonsmoker
- Labs: UA negative
- PVR: 75 mL

What other information would you want to know?

Therapeutic Discussion

- Behavioral
  - Already reducing fluid consumption
  - Has tried urge reduction
- Physiotherapy
  - Has done pelvic floor exercises since early 30s
- Pharmacologic
  - Has researched cognitive dysfunction and cannot agree to any impact on mentation

Additional Information

- She saw a PCP approximately 1 year ago and was prescribed a medication that caused constipation
- She lives alone and is currently self-sufficient
- She is experiencing some short-term memory issues

Therapeutic Management

- Reasons for selecting a beta-3 vs anti-muscarinic agents
  - Patient preferences
  - Concern of cognitive issues
  - Medication interaction
- Beta-3, vibegron would be an appropriate option for this patient

Stay tuned for our Q&A

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