UPDATES IN OVERACTIVE BLADDER

Christy Wilson PA-C, MPAS

Wellstar

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DISCLOSURE

- *I have no relevant relationships with ineligible companies to disclose within the past 24 months*

OBJECTIVES

- At the conclusion of this session participants should be able to:
  - Definition of OAB/ Urge urinary incontinence
  - Discuss signs and symptoms of OAB and how to recognize it in clinical practice
  - Discuss Treatment options
    - Behavioral
    - Medications
    - Procedures / surgical
  - Beers Criteria and why it is important to known when treating OAB
  - Case Studies for review

OVERACTIVE BLADDER

- "urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of UTI or other obvious pathology"
- Self limiting
- Clinical diagnosis

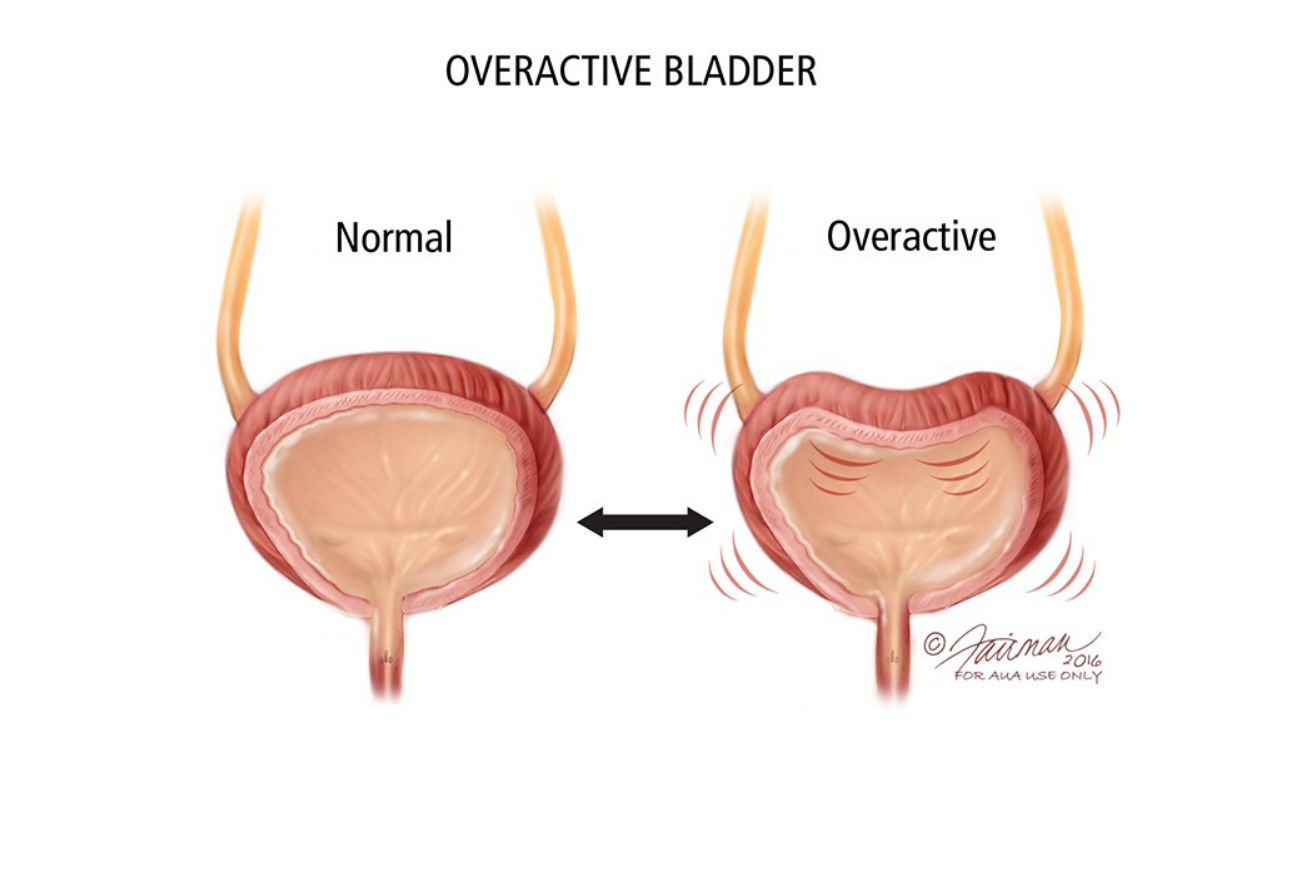
IUGA (International Urogynecological Association) and ICA (International Continence Society)

- Prevalence – up to 27% men / 47% women (AUA guidelines 2019)
- Pathophysiology: abnormal urothelium and suburothelial signaling that leads to pathologic sensation of urgency

Liu, Bonnie et al. Drug Therapy for Overactive Bladder. AUA Update Series 2021, Vol 40 page 193.

OVERACTIVE BLADDER (OAB)

- Definition
  - Syndrome described as having symptoms of urgency to urinate with or without incontinence, nocturia, and urinary frequency
  - NOT a disease but a group of symptoms
  - Different from stress urinary incontinence (SUI)
  - Can be associated with Urge Urinary Incontinence (UUI)



Lukacz, et al. Urgency urinary incontience/overactive bladder in females: Treatment; Up-to-date Accessed 2/14/2022.
https://www.urologyhealth.org/urology-a-z/o/overactive-bladder-(oab)

URGE URINARY INCONTINENCE

- Definition
  - Urge to void immediately and often associated with involuntary urine leakage
  - Temporary or persistent
  - Quality of life

QUESTIONNAIRE FOR PATIENTS

Name: _____Date:_____ MRN #_____

OAB-q short form symptom bother

This questionnaire asks about how much you have been bothered by selected bladder symptoms during the past 4 weeks. Please place a ✓ or ✗ in the box that best describes the extent to which you were bothered by each symptom during the past 4 weeks. There are no right or wrong answers. Please be sure to answer every question.

During the past 4 weeks, how bothered were you by. . .	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**A great deal**	**A very great deal**
1. An uncomfortable urge to urinate?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
2. A sudden urge to urinate with little or no warning?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
3. Accidental loss of small amounts of urine?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
4. Nighttime urination?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
5. Waking up at night because you had to urinate?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
6. Urine loss associated with a strong desire to urinate?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

SYMPTOMS

- Urgency with urination
- Urge urinary incontinence (Wet OAB)
- Difficult to control urination
- Frequency of urination usually > 8 x in 24 hr period
- Nocturia 2+ per night

- Worsens with age
- Prevention: healthy weight / exercise / limit caffeine and etoh / no smoking / pelvic floor exercises

CASE STUDY

- Mrs LUTs is a 57 yo female with known hx of depression and generalized anxiety disorder who is a mother of 2 kids.
  - Smokes ½ ppd but trying to cut back
  - 2 vaginal deliveries Full Term
  - Medications: escitalopram / clonazepam
- CC: Urge urinary incontinence worsening x 3 years with rare SUI (stress urinary incontinence) only when she laughs a lot
- OAB questionnaire
- UA micro negative / PVR 2 ml / cystoscopy normal without evidence of pelvic organ prolapse

CASE STUDY

- Discussed behavioral modifications / Bladder training
- Healthy bladder diet
- She is NOT interested in pelvic floor PT
- Insists she needs something because she "CANNOT LIVE LIKE THIS"
- What to do?

CASE STUDY

- Treatment:
  - Healthy bladder diet / pelvic floor exercises
  - Rx Virbegron 75 mg daily
- Mrs LUTS calls the clinic stating the medication was $400 and she cannot afford d/t her shopping habits
- Rx tropism ER 60 mg daily
  - Take on empty stomach
  - FU in 6-8 weeks

CASE STUDY

- Follow up appointment
  - PVR 0 ml
  - Some improvement in urgency / frequency / leakage
  - Continue to encourage behavioral modifications
  - Next steps

OAB WORKUP

- Voiding Diary
- Urinalysis / Urine cx
- No role for urodynamic study / cystoscopy / imaging in the initial workup

FIRST LINE THERAPY

- Behavioral Modifications
  - Diet
  - Bladder Training (change bladder habits)
  - Pelvic Floor Exercises / referral to PT
  - Weight loss
  - vaginal atrophy – topical estrogen cream
  - Timeframe – 6-12 weeks

Lukacz, E et al. Urgency Urinary incontinence / overactive bladder in females: Treatment www.uptodate.com accessed 2/12/2022

SECOND LINE THERAPY

- Medications
  - Anti-muscarinic agents
    - ER (extended-release medications preferred)
    - Higher risk of dementia
  - Beta 3 adrenergic agonists
    - **$$$**
  - COMBO
  - Takes up to 12 weeks to notice full effects
  - Risk of urinary retention, monitor with PVR

PHARMACOLOGICAL TREATMENTS

- **Anti-muscarinic agents**
  - MOA – stimulates acetylcholine to reduce smooth muscle contraction in the bladder
  - Increase bladder capacity / decrease urgency
  - Generic options / cheaper
  - Can cause cognitive dysfunction
  - Side Effects: dry mouth and eyes, constipation
  - Contraindications
  - Examples: trospium / darifenacin

- **Beta 3 adrenergic agonists**
  - Mirabegron * (risk of HTN)
  - Vibegron
  - MOA – smooth muscle relaxation in the bladder
  - Less side effects compared to anti-muscarinic agents
  - $$$
  - Contraindications
    - Uncontrolled HTN
    - Child Pugh class B / ESRD GFR < 30
    - Flecainide / propafenone cannot take 50 mg dose

Liu, Bonnie et al. Drug Therapy for Overactive Bladder. AUA Update Series 2021, Vol 40 page 193.

ANTI-MUSCARINIC AGENTS

- **Oxybutynin / Tolterodine**
  - Comes in immediate or extended release
    - Prefer extended release to min. SE
  - Cheap / generic
  - Not well tolerated
- **Oxybutynin**
  - Highly lipophilic / ***crosses the blood brain barrier resulting in CNS adverse effects***
  - Can be given transdermal or ER dosing which decreases SE
  - Avoid in elderly

Liu, Bonnie et al. Drug Therapy for Overactive Bladder. AUA Update Series 2021, Vol 40 page 193.

AUA UPDATE SERIES 2021 OAB

- **Trospium**
  - less likely to pass the blood brain barrier / take at least ONE hour prior to food
  - Food significantly decreases bioavailability
  - M2 / M3
  - No need to adjust for hepatic dz / only AM NOT metabolized by CYp3A4
  - Study UK – patients who use AM (anti-musarinic agents) have 20% increased risk of Dementia in the future

Liu, Bonnie et al. Drug Therapy for Overactive Bladder. AUA Update Series 2021, Vol 40 page 193.

AUA UPDATE SERIES 2021 OAB

- Combo Beta 3 adrenergic agonists and AM drugs
  - Improvements in volume voided / frequency / urgency and QOL
- Role of PDE5 inhibitors
  - Tadalafil – FDA approved for LUTS in men with BPH

Liu, Bonnie et al. Drug Therapy for Overactive Bladder. AUA Update Series 2021, Vol 40 page 193.

PHARMACOLOGICAL TREATMENT

- Recommend Follow up 4-6 weeks after starting medication
- If no improvement – titrate medication / combo
  - Solifenacin / Trospium PLUS mirabegron
- If some improvement – titrate medication
- Obtain PVR – if >1/3 total voided amount watch closely
- Cannot tolerate side effects -> 3rd line therapy

BEERS CRITERIA

- American Geriatric Society updates Beers Criteria
  - Criteria:
    - Potentially inappropriate medications in older adults
    - Potentially inappropriate medications to avoid in older adults with certain conditions
    - Medications to be used with caution in older adults
    - Medication combinations that may lead to harmful interactions
    - List of medications that should be avoided / dosed differently in those with poor renal function

OAB AND BEER

- Updated in 2019
- Anticholinergics / Anti-muscarinic agents made the LIST
- Prescribe with caution in the elderly
  - anti-muscarinic agents are contraindicated in elderly on oral potassium supplements d/t slowing gastric motility
  - Trospium is considered the safest (lowest DDI – drug drug interactions)

AGS BEERS CRITERIA
FOR POTENTIALLY INAPPROPRIATE MEDICATION USE IN OLDER ADULTS

FROM THE AMERICAN GERIATRICS SOCIETY

This clinical tool, based on *The AGS 2012 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults (AGS 2012 Beers Criteria)*, has been developed to assist healthcare providers in improving medication safety in older adults. Our purpose is to inform clinical decision-making concerning the prescribing of medications for older adults in order to improve safety and quality of care.

Originally conceived of in 1991 by the late Mark Beers, MD, a geriatrician, the *Beers Criteria* catalogues medications that cause adverse drug events in older adults due to their pharmacologic properties and the physiologic changes of aging. In 2011, the AGS undertook an update of the criteria, assembling a team of experts and funding the development of the AGS 2012 *Beers Criteria* using an enhanced, evidence-based methodology. Each criterion is rated (quality of evidence and strength of evidence) using the American College of Physicians' Guideline Grading System, which is based on the GRADE scheme developed by Guyatt et al.

The full document together with accompanying resources can be viewed online at www.americangeriatrics.org.

INTENDED USE

The goal of this clinical tool is to improve care of older adults by reducing their exposure to Potentially Inappropriate Medications (PIMs).

- This should be viewed as a guide for identifying medications for which the risks of use in older adults outweigh the benefits.
- These criteria are not meant to be applied in a punitive manner.
- This list is not meant to supersede clinical judgment or an individual patient's values and needs. Prescribing and managing disease conditions should be individualized and involve shared decision-making.
- These criteria also underscore the importance of using a team approach to prescribing and the use of non-pharmacological approaches and of having economic and organizational incentives for this type of model.
- Implicit criteria such as the STOPP/START criteria and Medication Appropriateness Index should be used in a complementary manner with the 2012 AGS Beers *Criteria* to guide clinicians in making decisions about safe medication use in older adults.

The criteria are not applicable in all circumstances (eg, patient's receiving palliative and hospice care). If a clinician is not able to find an alternative and chooses to continue to use a drug on this list in an individual patient, designation of the medication as potentially inappropriate can serve as a reminder for close monitoring so that the potential for an adverse drug effect can be incorporated into the medical record and prevented or detected early.

TABLE 1: 2012 AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

Organ System/ Therapeutic Category/Drug(s)	Recommendation, Rationale, *Quality of Evidence (QE) & Strength of Recommendation (SR)*
Anticholinergics (excludes TCAs)	
First-generation antihistamines (as single agent or as part of combination products) ■ Brompheniramine ■ Carbinoxamine ■ Chlorpheniramine ■ Clemastine ■ Cyproheptadine ■ Dexbrompheniramine ■ Dexchlorpheniramine ■ Diphenhydramine (oral) ■ Doxylamine ■ Hydroxyzine ■ Promethazine ■ Triprolidine	**Avoid.** Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; increased risk of confusion, dry mouth, constipation, and other anticholinergic effects/toxicity. Use of diphenhydramine in special situations such as acute treatment of severe allergic reaction may be appropriate. *QE = High (Hydroxyzine and Promethazine), Moderate (All others); SR = Strong*
Antiparkinson agents ■ Benztropine (oral) ■ Trihexyphenidyl	**Avoid.** Not recommended for prevention of extrapyramidal symptoms with antipsychotics; more effective agents available for treatment of Parkinson disease. *QE = Moderate; SR = Strong*

PAGE 1 Table 1 (continued on page 2)

Table 1 (continued from page 1)

TABLE 1: 2012 AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

Organ System/ Therapeutic Category/Drug(s)	Recommendation, Rationale, *Quality of Evidence (QE) & Strength of Recommendation (SR)*
Antispasmodics ■ Belladonna alkaloids ■ Clidinium-chlordiazepoxide ■ Dicyclomine ■ Hyoscyamine ■ Propantheline ■ Scopolamine	**Avoid except in short-term palliative care to decrease oral secretions.** Highly anticholinergic, uncertain effectiveness. *QE = Moderate; SR = Strong*
Antithrombotics	
Dipyridamole, oral short-acting[a] (does not apply to the extended-release combination with aspirin)	**Avoid.** May cause orthostatic hypotension; more effective alternatives available; IV form acceptable for use in cardiac stress testing. *QE = Moderate; SR = Strong*
Ticlopidine[a]	**Avoid.** Safer, effective alternatives available. *QE = Moderate; SR = Strong*
Anti-infective	
Nitrofurantoin	**Avoid for long-term suppression; avoid in patients with CrCl <60 mL/min.** Potential for pulmonary toxicity; safer alternatives available; lack of efficacy in patients with CrCl <60 mL/min due to inadequate drug concentration in the urine. *QE = Moderate; SR = Strong*
Cardiovascular	
Alpha$_1$ blockers ■ Doxazosin ■ Prazosin ■ Terazosin	**Avoid use as an antihypertensive.** High risk of orthostatic hypotension; not recommended as routine treatment for hypertension; alternative agents have superior risk/benefit profile. *QE = Moderate; SR = Strong*
Alpha agonists ■ Clonidine ■ Guanabenz[a] ■ Guanfacine[a] ■ Methyldopa[a] ■ Reserpine (>0.1 mg/day)[a]	**Avoid clonidine as a first-line antihypertensive. Avoid others as listed.** High risk of adverse CNS effects; may cause bradycardia and orthostatic hypotension; not recommended as routine treatment for hypertension. *QE = Low; SR = Strong*
Antiarrhythmic drugs (Class Ia, Ic, III) ■ Amiodarone ■ Dofetilide ■ Dronedarone ■ Flecainide ■ Ibutilide ■ Procainamide ■ Propafenone ■ Quinidine ■ Sotalol	**Avoid antiarrhythmic drugs as first-line treatment of atrial fibrillation.** Data suggest that rate control yields better balance of benefits and harms than rhythm control for most older adults. Amiodarone is associated with multiple toxicities, including thyroid disease, pulmonary disorders, and QT interval prolongation. *QE = High; SR = Strong*
Disopyramide[a]	**Avoid.** Disopyramide is a potent negative inotrope and therefore may induce heart failure in older adults; strongly anticholinergic; other antiarrhythmic drugs preferred. *QE = Low; SR = Strong*
Dronedarone	**Avoid in patients with permanent atrial fibrillation or heart failure.** Worse outcomes have been reported in patients taking dronedarone who have permanent atrial fibrillation or heart failure. In general, rate control is preferred over rhythm control for atrial fibrillation. *QE = Moderate; SR = Strong*
Digoxin >0.125 mg/day	**Avoid.** In heart failure, higher dosages associated with no additional benefit and may increase risk of toxicity; decreased renal clearance may increase risk of toxicity. *QE = Moderate; SR = Strong*

PAGE 2 Table 1 (continued on page 3)

Rutman, Matthew P et al. "Overactive Bladder Prescribing Considerations: The Role of Polypharmacy, Anticholinergic Burden, and CYP2D6 Drug–Drug Interactions." Clinical drug investigation vol. 41,4 (2021): 293-302. doi:10.1007/s40261-021-01020-x

AUA BEERS LIST

Potentially Inappropriate Medication for Use in Older Adults (developed by the AUA Beers Criteria White Paper Workgroup based on [1]).

Medication	Urologic Indication
Nitrofurantoin	• Acute treatment of uncomplicated urinary tract infection without systemic symptoms in individuals living in communities with an identified high risk of quinolone-resistant organisms OR due to multiply-resistant bacteria with identified sensitivity to nitrofurantoin
Alpha-blockers	• Medical management of bothersome benign prostate enlargement symptoms while monitoring for efficacy and adverse events
Estrogenics	• Topical (vaginal) use for symptomatic vaginal atrophy due to low estrogenic states • Risk reduction for chronic recurrent urinary tract infections in post-menopausal women
Anti-muscarinics	• Trial of antimuscarinics is appropriate as second line therapy in patients with high bother from overactive bladder symptoms, with monitoring of benefits, risks, and adverse effects for that individual patient[27] • Trial of antimuscarinics is appropriate for male patients with benign prostatic enlargement in whom the symptom complex includes high bother from urgency and frequency symptoms in the absence of significant urinary retention (post-void residual urine volume <200 mL) and in patients for whom first-line therapy for OAB fails[27]

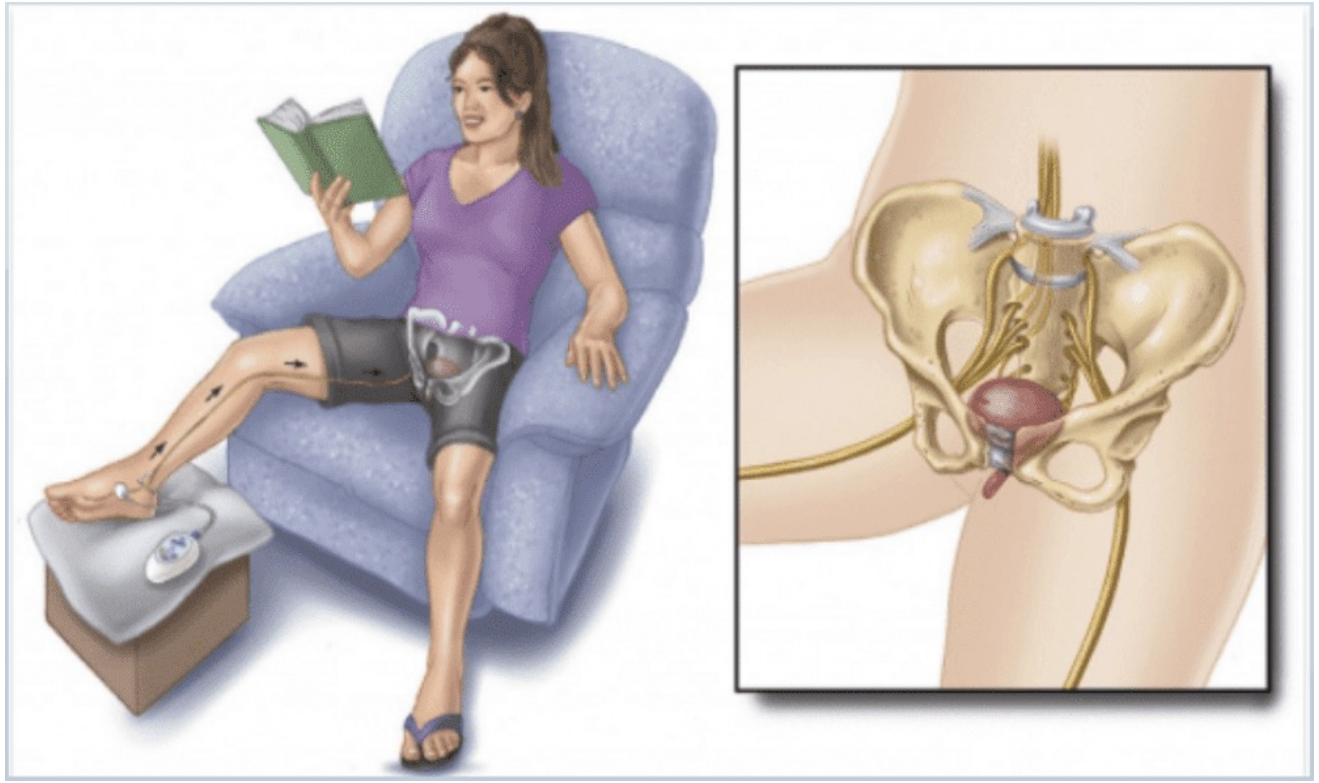
https://www.auanet.org/guidelines/guidelines/beers-criteria

THIRD LINE THERAPY

- PTNS
- Botox

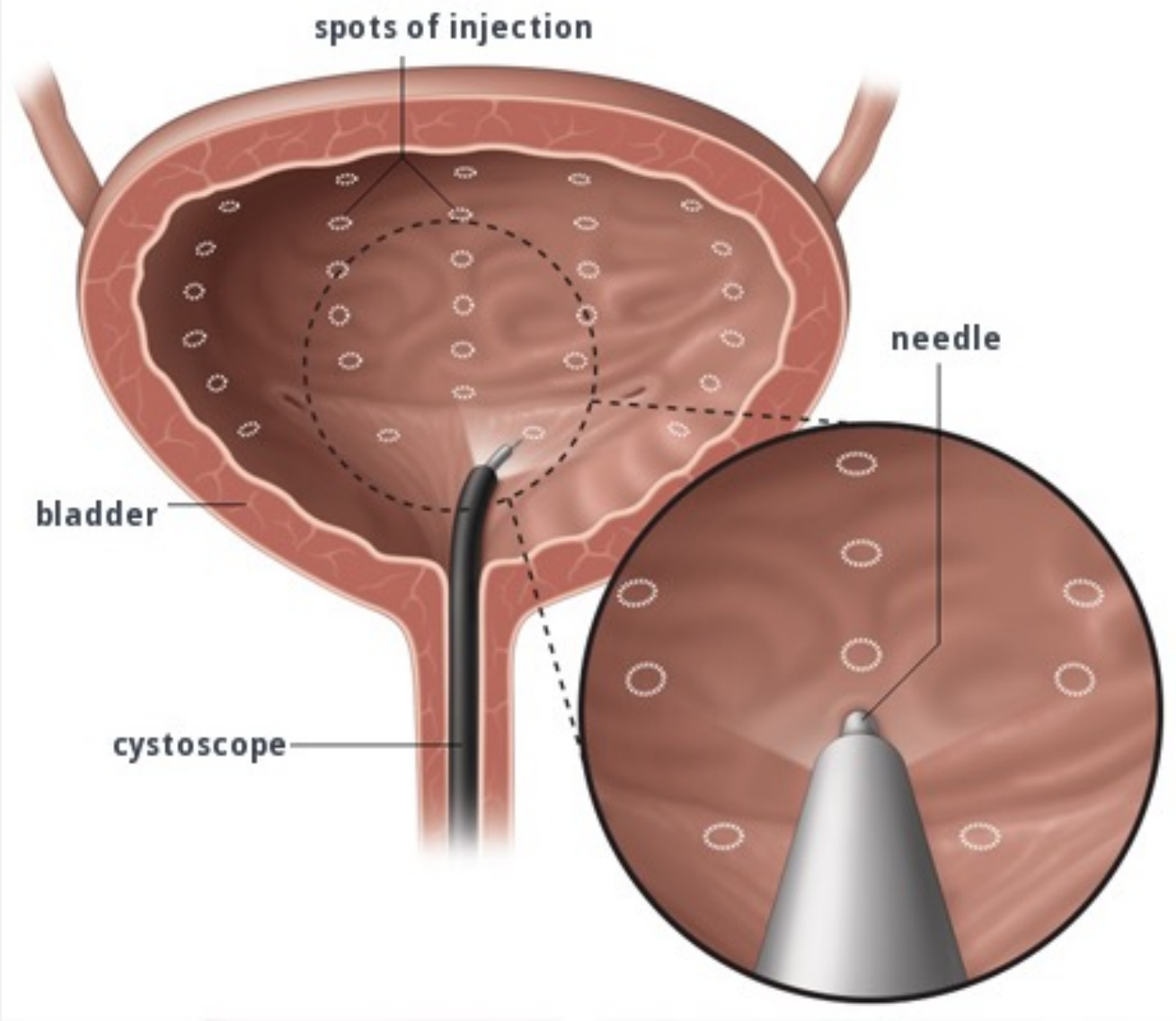
PTNS

- PTNS – Peripheral tibial nerve stimulation
  - Less invasive
  - Acupuncture-like electrical nerve stimulation
  - Weekly for 12 weeks / 30 minutes each session
  - Needle placed medially behind the ankle with mild electrical stimulation
  - Shown to reduce OAB s/sx and improve quality of life



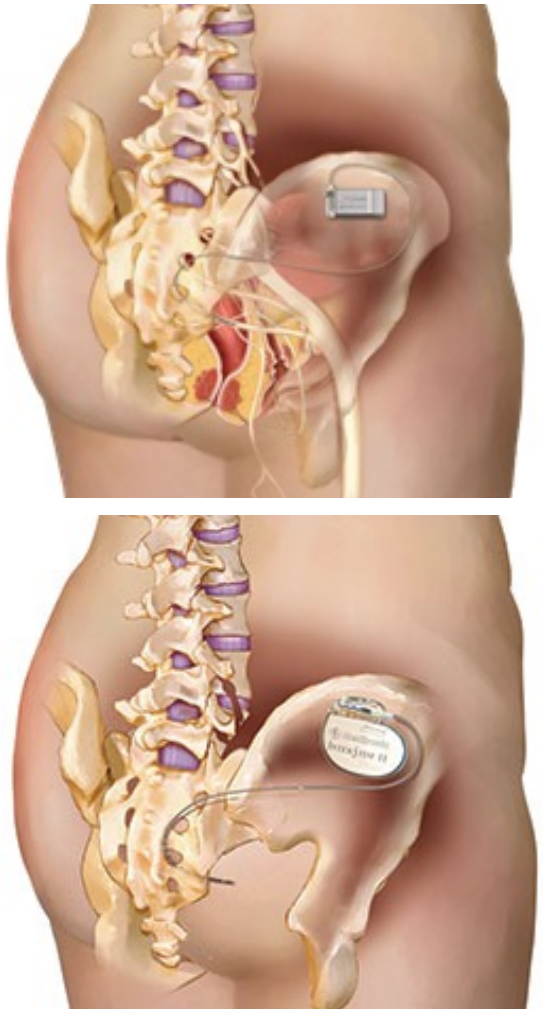
BOTOX

- Botulinum toxin
  - Consider if failed pharmacologic therapy
  - Botox administered under local anesthesia
  - Results are seen within 2 weeks and last for 3-12 months
  - Can cause increased risk of UTIs



FORTH LINE THERAPY

- Sacral Neuromodulation
  - Min. invasive surgical electrical stimulation
  - InterStim / Axonics
  - Patients must be able to learn to adjust the setting with a small device
  - Wire is placed into S3 foreman and connected to stimulation device
    - Two phase procedure
      - Test phase – need to see > 50% improvement in S/sx
      - Second stage implantation phase



CASE STUDY

- 74 yo male with hx of BPH with LUTS (lower urinary tract symptoms)
  - PMHx: HTN BMI 32
  - Workup / GU history
    - Urodynamic study showed bladder outlet obstruction
    - PVR 35 ml
    - Prostate US 55 cc
    - I-PSS score 25/35 Q 4
  - S/p TURP 12/2020 / path benign

INTERNATIONAL PROSTATE SYMPTOM SCORE

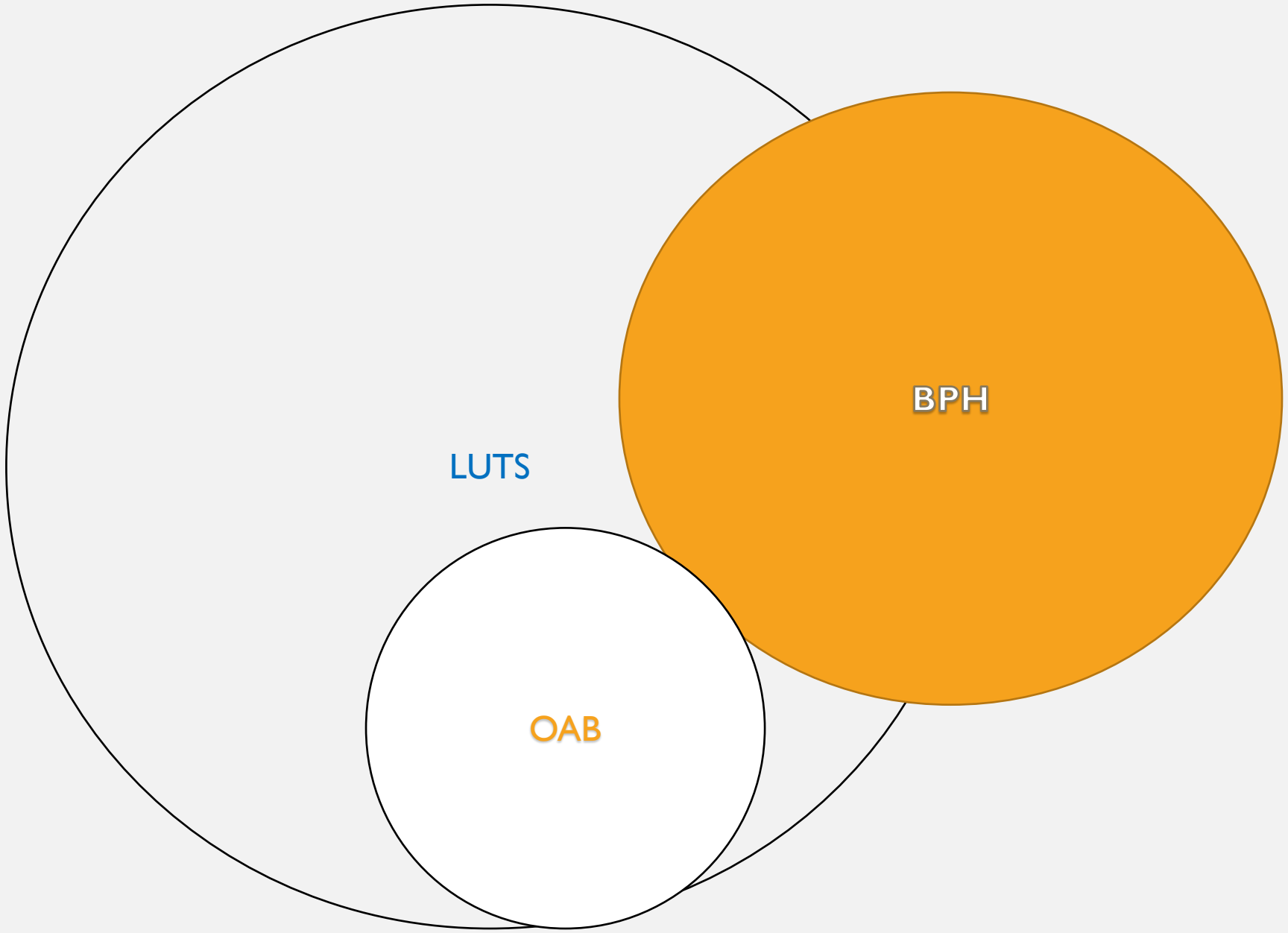
International Prostate Symptom Score (I-PSS)

Patient Name: _____ **Date of birth:** _____ **Date completed** _____

In the past month:	Not at All	Less than 1 in 5 Times	Less than Half the Time	About Half the Time	More than Half the Time	Almost Always	Your score
1. Incomplete Emptying How often have you had the sensation of not emptying your bladder?	0	1	2	3	4	5	
2. Frequency How often have you had to urinate less than every two hours?	0	1	2	3	4	5	
3. Intermittency How often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Urgency How often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Weak Stream How often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Straining How often have you had to strain to start urination?	0	1	2	3	4	5	
	None	**1 Time**	**2 Times**	**3 Times**	**4 Times**	**5 Times**	
7. Nocturia How many times did you typically get up at night to urinate?	0	1	2	3	4	5	
Total I-PSS Score							

Score: 1-7: *Mild* 8-19: *Moderate* 20-35: *Severe*

Quality of Life Due to Urinary Symptoms	Delighted	Pleased	Mostly Satisfied	Mixed	Mostly Dissatisfied	Unhappy	Terrible
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?	**0**	**1**	**2**	**3**	**4**	**5**	**6**


LUTS
BPH
OAB

CASE STUDY

- Initially did very well with TURP but 6+ months later developed increasing frequency / urgency and severe urge incontinence with some lack of sensory awareness
- 3 depends a day / accidents
- Effected his quality of life
- I-PSS 15/35 (urgency / frequency / nocturia)

- Treatment options

CASE STUDY

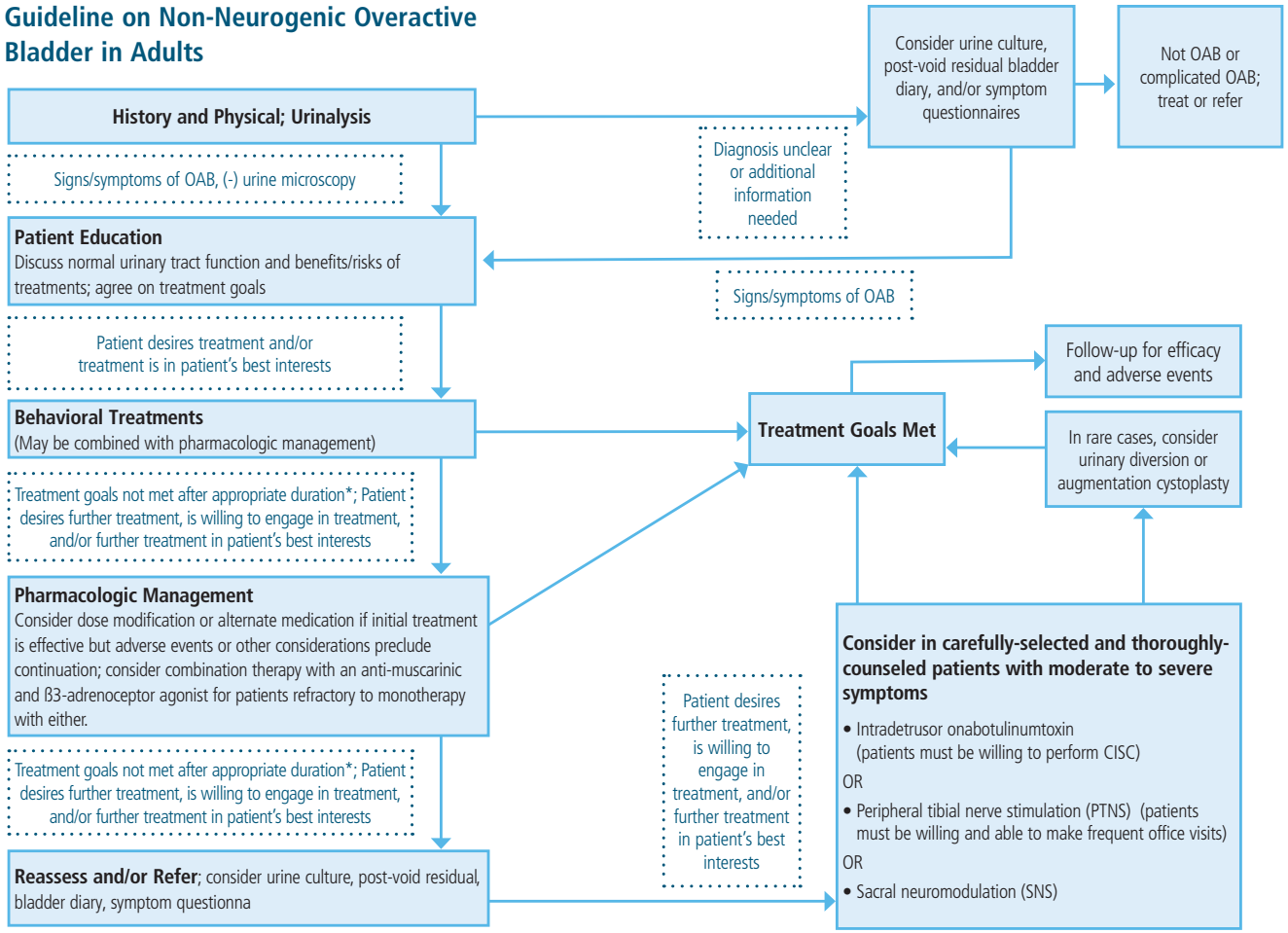
- Behavioral Modifications / weight loss
- Started on mirabegron 25 mg x 2 months
- No significant improvement
- Discussed 3rd line therapies Botox / PTNS
- Elected to proceed with PTNS

Patient agreed to [illegible] is picture taken for this presentation

PTNS

- Prior to starting PTNS
  - Voids 5-6x a day
  - 3-4x nocturia
  - High Urgency
  - Severe urge urinary incontinence / 3 depends daily / daily accidents
- After completing 12 weekly sessions
  - Voids 4-5x a day
  - 1x nocturia
  - 1 depends a day, sometimes stays dry
  - Mild urgency

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.

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

CLINICAL PEARLS

- When to refer to urology?
  - No response with 1st line therapy
  - Neurological disease
  - Hematuria / pelvic mass / underlying disease that could be contributing
- OAB is a clinical diagnosis
- Treatment plans:
  - require shared decision making
  - step by step approach
  - individualized
- Screen for Dementia in OAB patients

REFERENCES

- AUA Guidelines OAB Adults 2019
- https://www.auanet.org/guidelines/guidelines/beers-criteria
- Rutman, Matthew P et al. "Overactive Bladder Prescribing Considerations: The Role of Polypharmacy, Anticholinergic Burden, and CYP2D6 Drug–Drug Interactions." Clinical drug investigation vol. 41,4 (2021): 293-302. doi:10.1007/s40261-021-01020-x
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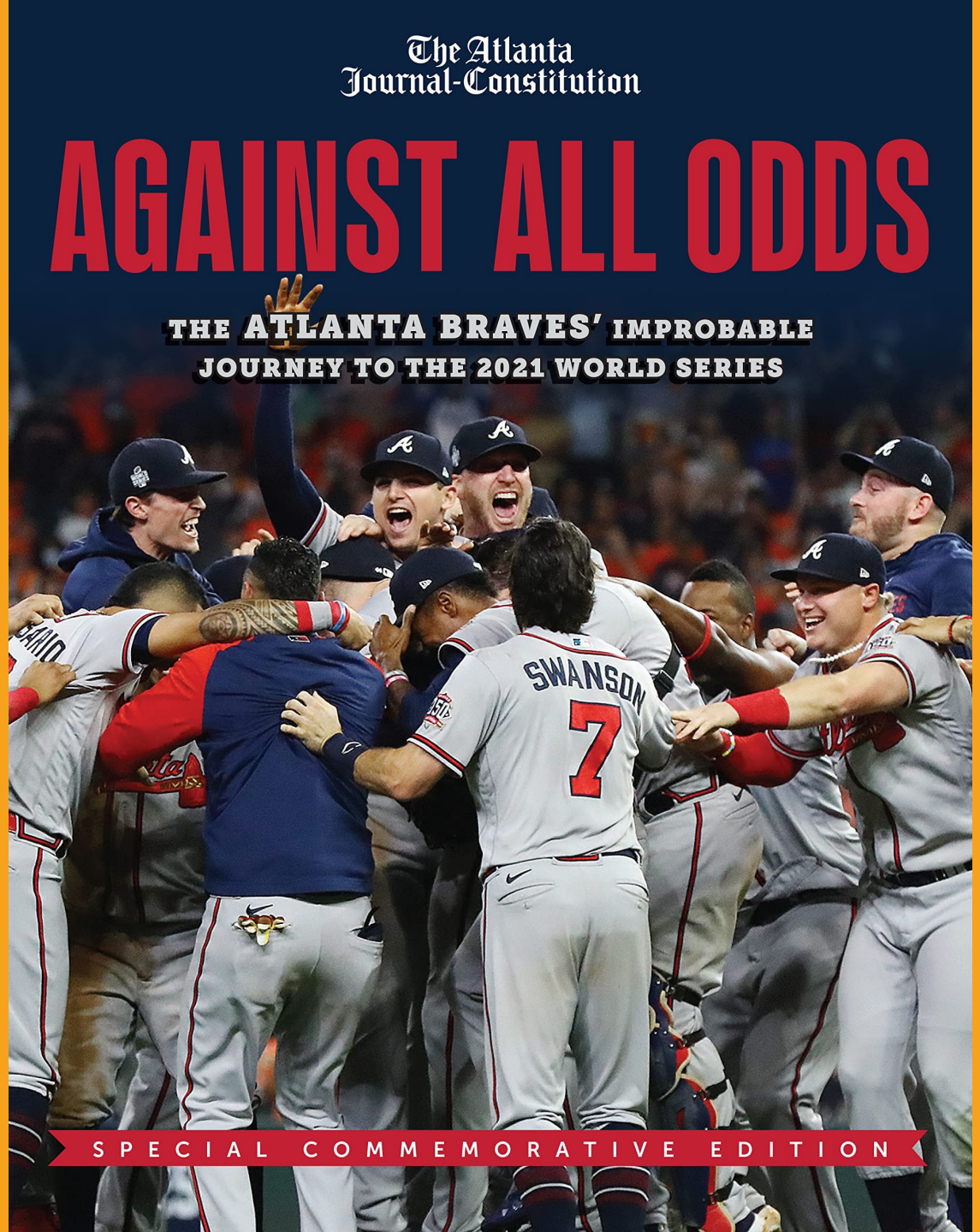
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