



Association of  
Reproductive  
Health  
Professionals

*A Quick Reference Guide  
for Clinicians®*

## Diagnosis and Management of Overactive Bladder

### Contents

Using This Guide	3
Introduction to Overactive Bladder	5
Diagnosis	11
Non-Pharmacologic Treatment	17
Pharmacologic Treatment	21
Counseling Tips	33
Resources for Patients	36

## Clinical Advisory Committee

### **Roxanne Jamshidi, MD, MPH**

Assistant Professor  
Department of Ob/Gyn  
Johns Hopkins University  
Baltimore, MD

### **Anne Moore, APN, WHNP-BC, ANP-BC, FAANP**

Professor of Nursing  
Vanderbilt University School of Nursing  
Nashville, TN

### **Amy Park, MD**

Staff  
Female Pelvic Medicine and Reconstructive Surgery  
Washington Hospital Center  
Washington, DC

## Contributing Staff /Consultants

Jerry Blaivas, MD  
Consulting Medical Writer

Camille V. Harris, MPH  
ARHP Program Manager

Ellen Cohen, CertEd, DipEd, CCMEP  
ARHP Director of Education

Diane Shannon, MD, MPH  
Medical Writer

Beth Jordan, MD  
ARHP Medical Director

Wayne C. Shields  
ARHP President and CEO

## Financial Disclosure Information

The following committee members and/or contributing staff have a financial interest or affiliation with the manufacturers of commercial products possibly related to topics covered in this *Quick Reference Guide*. These financial interests or affiliations are in the form of grants, research support, speaker support, or other support. This support is noted to fully inform readers and should not have an adverse impact on the information provided within this publication.

**Moore:** Consultant for Bayer HealthCare Pharmaceuticals and Teva Women's Health

**Blaivas, Cohen, Jamshidi, Jordan, Harris, Park, Shannon, and Shields** have no relationships to disclose.

*This publication is funded through educational grants from Allergan, Inc., Astellas Pharma Inc., and Pfizer.*

## Using This Guide

Overactive bladder (OAB) is a common condition that adversely affects the quality of life of approximately 17 percent of adults worldwide.<sup>1,2</sup> Characterized by lower urinary tract symptoms including urinary frequency, urgency with or without incontinence, and nocturia, OAB is believed to be due to detrusor overactivity and changes in the afferent nerve endings in the bladder.<sup>3-5</sup> In the past, treatment for the condition was generally ineffective. For this reason and a host of patient-related and clinician-related factors, many patients suffered with OAB for years without resolution.

Fortunately, treatment is now available that can improve the symptoms of OAB. Combined with behavioral techniques, pharmacologic therapy can help patients regain control of OAB symptoms and return to more fully active lives. The initial diagnosis and treatment of OAB can be managed effectively by primary care providers, with referral to specialist care for refractory cases or when presentation or test results suggest a more complex clinical scenario. Indeed, because of the greater awareness of the availability of effective treatment, primary care providers increasingly are managing OAB treatment.

Primary care providers can play an essential role in managing OAB by identifying patients whose symptoms are consistent with the condition, promptly diagnosing and treating the disorder, and referring patients to specialists as necessary. This *Quick Reference Guide for Clinicians* is designed to help health care providers more easily identify and treat patients with OAB.

Considering the possibility that a woman's symptoms may represent OAB is the crucial first step in diagnosing the condition. We hope this *Quick Reference Guide for Clinicians* allows health care providers to confidently take the first steps in diagnosis and treatment, shortening the suffering of the many women who live with the condition.

The following abbreviations are used throughout this document:

BID—twice daily

ER—extended release

IR—immediate release

LUTS—lower urinary tract symptoms

OAB—overactive bladder

QD—once daily

SUI—stress urinary incontinence

TID—three times daily

UTI—urinary tract infection

UUI—urge urinary incontinence

## References

1. Milsom I, Abrams P, Cardozo L, et al. How widespread are the symptoms of an overactive bladder and how are they managed? A population-based prevalence study. *BJU Int.* 2001;87(9):760-6.
2. Stewart WF, Van Rooyen JB, Cundiff GW, et al. Prevalence and burden of overactive bladder in the United States. *World J Urol.* 2003;20(6):327-36.
3. Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn.* 2002;21(2):167-78.
4. Yoshida M, Masunaga K, Nagata T, et al. The forefront for novel therapeutic agents based on the pathophysiology of lower urinary tract dysfunction: pathophysiology and pharmacotherapy of overactive bladder. *J Pharmacol Sci.* 2010;112(2):128-34.
5. Michel MC, Chapple CR. Basic mechanisms of urgency: roles and benefits of pharmacotherapy. *World J Urol.* 2009;27(6):705-7.

# Introduction to Overactive Bladder

## Overview

- Overactive bladder (OAB) is a term first used in the 1990s to describe a constellation of lower urinary tract symptoms (LUTS).
- OAB is prevalent and significantly affects patients' quality of life.

## Definitions

- OAB is urinary urgency (with or without urinary incontinence), urinary frequency, and nocturia, in the absence of proven infection or other obvious pathology.<sup>1</sup>
- Urinary urgency is a compelling urge to urinate that is difficult to defer.<sup>2</sup>
- Urinary frequency is defined as voiding more than eight times in 24 hours.<sup>3,4</sup>
- Nocturia is defined as awakening more than one time per night to void.<sup>5</sup>

## Pathophysiology

- The symptoms of OAB are suggestive of urodynamically demonstrable detrusor overactivity, although they can be due to other forms of urethro-vesical dysfunction.<sup>1</sup>
- OAB is also thought to result from changes in the afferent nerve endings in the bladder that increase bladder sensation.<sup>6</sup>

## Prevalence

- Approximately 17 percent of adults more than 18 years old have OAB.<sup>7-9</sup>
- The prevalence of OAB increases with age among both men and women.<sup>8</sup>
- One third of patients with OAB have incontinence.<sup>8</sup>
- As many as 45 percent of women will have urinary incontinence in their lifetime.<sup>10</sup>

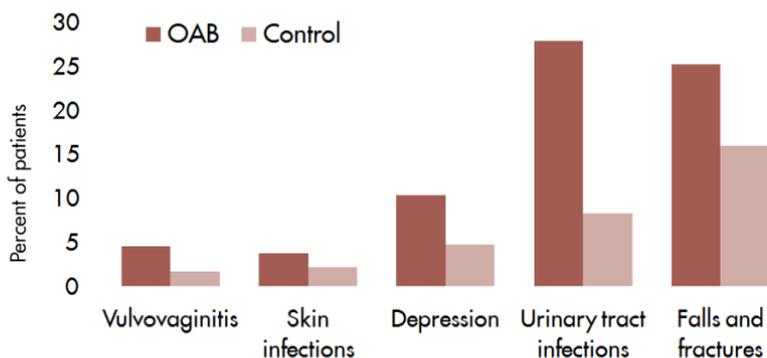
## Types of urinary incontinence

- Urge urinary incontinence (UUI) is incontinence characterized by a compelling need to urinate
- Stress urinary incontinence (SUI) is incontinence during sudden increases in intra-abdominal pressure (cough, sneeze)
- Mixed urinary incontinence is a combination of stress and urge incontinence

## Comorbid conditions

- Several conditions are significantly more frequent among patients with OAB than among control subjects; the most prevalent comorbidities are urinary tract infections (UTIs), falls, and fractures.<sup>11</sup>

Figure 1: Prevalence of OAB comorbidities<sup>11</sup>



- In one study:<sup>12</sup>
  - Of women more than 65 years old who had urge incontinence at least once per week, 19 to 42 percent sustained falls.
  - Fractures occurred in 4 to 9 percent of these falls.
  - Frequent urge incontinence was an independent risk factor for falling (OR = 1.26).

## Impact of incontinence

- Impact on patients:

- Psychological—People with OAB may become depressed because of their symptoms, and some feel guilty. The embarrassment of leaking or smelling of urine can lead to a loss of self-respect and dignity.
- Social—OAB sufferers might restrict social activity outside the home for fear of leaking urine or because of the frequent need to use a toilet.
- Domestic—Some individuals with OAB use specialized undergarments and bedding materials for incontinence. These items can be costly and are not always covered by medical insurance.
- Occupational—Overactive bladder may lead to decreased productivity in the workplace. Some patients may avoid going to work for fear of leaking urine.
- Sexual—Women with OAB have reported avoiding dating and sexual intimacy because of overactive bladder symptoms and fear of leaking urine.
- Physical—Some physical activities like exercising might be limited because of the frequent need to urinate or fear of leaking urine.
- Impact on society:
  - Cost—\$12.6 billion was spent on therapy for OAB in 2000 (\$9.1 billion spent for community residents and \$3.5 billion for institutional residents).<sup>13</sup>

### Missed opportunities for treatment

- More than 50 percent of patients who seek treatment for OAB wait more than a year before seeing a health care provider.<sup>14,15</sup>
- Despite the widespread prevalence of OAB, its impact on quality of life, and its overall morbidity, this condition remains undiagnosed and undertreated for many patients.
  - Patient-related causes:<sup>7,16,17</sup>
    - Embarrassment
    - Failure to see symptoms as abnormal

- Belief that symptoms are self-limited
- Perception of lack of treatment efficacy
- Fear of procedure
- Fear of cost of treatment
- Clinician-related causes: <sup>7,16,17</sup>
  - Misperception that symptoms are not important to the patient (perhaps because the patient does not volunteer information or complaints)
  - Misperception that OAB is a natural part of aging
  - Misperception that treatment is ineffective
  - Lack of awareness of the differential diagnosis
  - Lack of appreciation for the impact on quality of life
  - Failure to consider potential complications, including:
    - Depression
    - Skin infections
    - Falls and fractures

### Differential diagnosis in women

- There are a limited number of ways the bladder can express its pathology.
- Thus, the symptoms seen with OAB can have a number of different underlying causes, including:<sup>18</sup>
  - Uro-gynecologic conditions
    - Bladder cancer
    - Neurogenic bladder
    - Interstitial cystitis
    - Pelvic organ prolapse
    - Postsurgical complication
    - Stress incontinence
    - Urethral diverticulum

- Urinary tract infection
- General medical conditions
  - Polyuria/polydipsia
  - Diabetes
  - Congestive heart failure
  - Medications

**Table 1: Differential diagnosis by symptoms**

Symptoms	OAB	SUI	UTI
Urgency	Yes	No	Yes
Frequency	Yes	No	Yes
Leaking during physical activity	Sometimes	Yes	No
Amount of leakage	Variable	Variable	Small
Urge incontinence	1/3	No	Sometimes
Nocturia	Usually	Sometimes	Usually
Urinalysis & culture	Normal	Normal	Abnormal

- A simple symptom assessment can help differentiate among OAB, stress incontinence, and urinary tract infection.
- Both OAB and UTI are accompanied by urinary urgency, frequency, and urge incontinence, but most patients with UTI also have dysuria, and all have pyuria or hematuria and a positive urine culture.
- Stress incontinence is not a symptom of OAB, but about one third of patients with SUI also have urge incontinence.<sup>19</sup>

## References

1. Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn*. 2002;21(2):167-78.
2. Chapple C. Classification of mixed incontinence. *Eur Urol*. 2006;5(16)837-41.
3. Fitzgerald MP, Brubaker L. Variability of 24-hour voiding diary variables among asymptomatic women. *J Urol*. 2003;169(1):207-9.
4. Fitzgerald MP, Stablein U, Brubaker L. Urinary habits among asymptomatic women. *Am J Obstet Gynecol*. 2002;187(5):1384-8.
5. van Kerrebroeck P, Abrams P, Chaikin D, et al. The standardisation of terminology in nocturia: report from the standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn*. 2002;21:179-83.
6. Yoshida M, Masunaga K, Nagata T, et al. The forefront for novel therapeutic agents based on the pathophysiology of lower urinary tract dysfunction: pathophysiology and pharmacotherapy of overactive bladder. *J Pharmacol Sci*. 2010;112(2):128-34.
7. Milsom I, Abrams P, Cardozo L, et al. How widespread are the symptoms of an overactive bladder and how are they managed? A population-based prevalence study. *BJU Int*. 2001;87(9):760-6.
8. Stewart W, Herzog R, Wein A. The prevalence and impact of overactive bladder in the U.S.: results from the NOBLE program. *Neurourol Urodyn*. 2001;20:406-8.
9. Stewart WF, Van Rooyen JB, Cundiff GW, et al. Prevalence and burden of overactive bladder in the United States. *World J Urol*. 2003;20(6):327-36.
10. Buckley BS, Lapitan MC; Epidemiology Committee of the Fourth International Consultation on Incontinence, Paris, 2008. Prevalence of urinary incontinence in men, women, and children—current evidence: findings of the Fourth International Consultation on Incontinence. *Urology*. 2010;76(2):265-70.
11. Darkow T, Fontes CL, Williamson TE. Costs associated with the management of overactive bladder and related comorbidities. *Pharmacotherapy*. 2005;25(4):511-9.
12. Brown JS, Vittinghoff E, Wyman JF, et al. Urinary incontinence: does it increase risk for falls and fractures? Study of Osteoporotic Fractures Research Group. *J Am Geriatr Soc*. 2000;48(7):721-5.
13. Hu TW, Wagner TH, Bentkover JD, et al. Costs of urinary incontinence and overactive bladder in the United States: a comparative study. *Urology*. 2004;63(3):461-5.
14. Harris Interactive. Harris Interactive survey examines a not-so-talked-about health issue affecting intimacy for many. *Health Care News*. June 7, 2001; 1(18).
15. Dmochowski RR, Newman DK. Impact of overactive bladder on women in the United States: results of a national survey. *Curr Med Res Opin*. 2007;23(1):65-76.
16. Milsom I, Stewart W, Thüroff J. The prevalence of overactive bladder. *Am J Manag Care*. 2000;6(11 Suppl):S565-73.
17. Ricci JA, Baggish JS, Hunt TL, et al. Coping strategies and health care-seeking behavior in a US national sample of adults with symptoms suggestive of overactive bladder. *Clin Ther*. 2001;23(8):1245-59.
18. Rosenberg MT, Newman DK, Tallman CT, Page SA. Overactive bladder: recognition requires vigilance for symptoms. *Cleve Clin J Med*. 2007;74(Suppl 3):S21-9.
19. Abrams P, Wein AJ. *The Overactive Bladder: A Widespread and Treatable Condition*. Stockholm, Sweden: Erik Sparre Medical AB; 1998.

# Diagnosis

## Presentation

- OAB generally presents in one of three ways:
  - The patient states, “I have OAB,” because she is familiar with the term from advertisements, the Internet, other patients, or other health care providers.
  - The patient offers a complaint of LUTS that the health care provider interprets as OAB.
  - Upon querying, the patient admits to OAB symptoms.

## Diagnostic evaluation

- The key components of the diagnostic evaluation of OAB include a history, a questionnaire, a physical examination, urinalysis, possibly with urine culture, and a bladder diary.
- The evaluation should begin with a focused history and questionnaire, as well as a focused physical exam, including a vaginal exam.
- A urinalysis should be conducted for all patients with OAB symptoms.
- A urine culture should be sent if the history and physical exam suggest a possible UTI.
- Patients should be instructed in how to keep a bladder diary (see page 14).

### Lower Urinary Tract Symptoms

LUTS can be divided into symptoms that occur during bladder storage and during voiding:

- Storage-related symptoms
  - Urinary frequency
  - Urgency
  - Nocturia
  - Incontinence
  - Pain
- Voiding-related symptoms
  - Hesitancy, weak stream, or straining
  - Incomplete emptying
  - Pain
  - Post-void dribbling

## Focused history and questionnaire

- During the focused history and questionnaire, the health care provider should ask about LUTS, as well as the presence or absence of:
  - Diabetes
  - Neurologic disorders
  - Recurrent UTI
  - Hematuria
  - Kidney stones
  - Previous lower abdominal or pelvic surgery
  - Pelvic organ prolapse
  - Vaginitis

## Focused physical exam

- The focused physical exam should include evaluation of these functional areas, as they pertain to the urinary system:
  - General
  - Neurologic
  - Urologic/gynecologic
  - Neuro-urologic

## Vaginal exam

- During the vaginal exam, the provider should:
  - Assess perineal sensation and reflexes
  - Assess post-void residual volume

### Pelvic Organ Prolapse

Pelvic organ prolapse is defined as vaginal protrusion of the pelvic organs past their normal anatomic positions. The examination for pelvic organ prolapse is most conveniently performed in the dorsal lithotomy position with a full bladder. The provider asks the patient to push and strain down and assesses the degree of descent, using the remnants of the hymenal ring as a reference point for the grading system.

Pelvic organ prolapse is a potentially remediable cause of OAB.<sup>1</sup> A patient with pelvic organ prolapse also may experience overflow incontinence, in which urethral “kinking” caused by the prolapse results in incomplete emptying and quicker filling of the bladder.

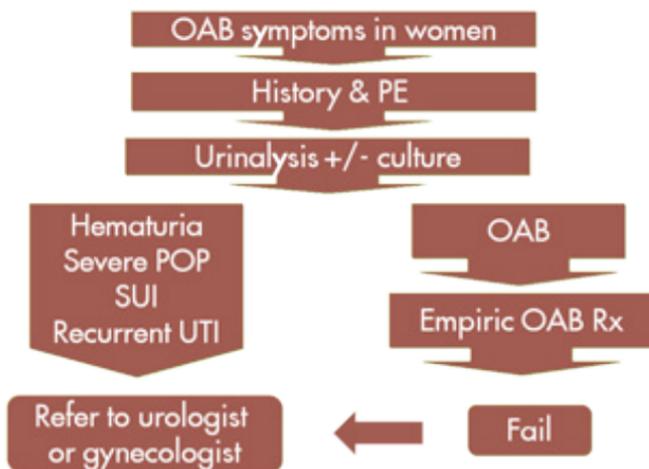
The Baden-Walker Classification of prolapse is delineated here:<sup>2</sup>

- Grade 0 - No descent
- Grade 1 - Descent halfway to the hymen
- Grade 2 - At the hymen
- Grade 3 - Halfway past the hymen
- Grade 4 - > halfway past the hymen

- Palpate for masses or tenderness
- Examine for atrophic vaginitis, pelvic organ prolapse, and urethral diverticulum

### Algorithm for OAB management

- Women with hematuria, advanced pelvic organ prolapse (i.e., grade 3 or 4), SUI, or recurrent UTIs should be referred to a urologist or gynecologist for further workup.
- Women without these conditions should be treated empirically for OAB.
- Women for whom empiric treatment fails should be referred for further workup.



## Bladder diary

The bladder diary can be a very useful tool for diagnosis and management decisions for the treatment of OAB. The figure shows one version of a bladder diary. (An electronic version of a similar diary from the National Institute of Diabetes and Digestive and Kidney Diseases, which is available for download, is listed in the Patient Resources section of this *Quick Reference Guide*.)

- In the first column, the patient records the time of each urination or incontinent episode.
- In the second column, she records the reason she voided, using the Urgency Perception Score (see below).
- In the third column, she records the measured amount of urine.
- In the fourth column, she records the amount of incontinence.

### Urgency Perception Score<sup>3</sup>

Health care providers can use this questionnaire to assess the severity of urinary urgency.

*Please select the number next to your answer and use it for your response to the questions.*

#### (a) Why did you urinate?

- (0) out of convenience (no urge or desire)
- (1) because I have a mild urge (but can delay urination for more than an hour if I have to)
- (2) because I have a moderate urge (but can delay urination for more than 10 but less than 60 minutes if I have to)
- (3) because I have a severe urge (but can delay urination for less than 10 minutes)
- (4) because I have a desperate urge (must stop what I am doing and go immediately)

#### (b) Incontinence grade

- (0) Grade 1 – some drops
- (1) Grade 2 – moderate loss (wet underwear)
- (2) Grade 3 – severe loss (wet outer clothes)

Name: \_\_\_\_\_ Date: \_\_\_\_\_

Time of day started: \_\_\_\_\_  AM  PM

Time you went to bed: \_\_\_\_\_

Time you got up for the day: \_\_\_\_\_

Time of Urination and/ or Incontinence Episode	Why did you urinate at this time (see question (a) for responses)	Amount of urination (measure with a cup in cc's, ml's, or ounces)	Incontinence grade (see question (b) for responses)
1)			
2)			
3)			
4)			
5)			
6)			
7)			
8)			
9)			
10)			
11)			
12)			
13)			
14)			
15)			

## Normal Voiding Amounts

In order to evaluate the data in the bladder diary, it is important to be familiar with normal voiding values.

- Mean 24-hour urinary output (both men and women):<sup>4</sup> 1700 ml
- Mean number of voids:<sup>4</sup> 6 to 7
- Mean bladder capacity:<sup>4</sup> 330 ml (although there is great variability among individual patients, 300 to 700 ml is considered the normal range)

Table 2. Normal voiding amounts<sup>4</sup>

Variable	All Patients Mean (Median)	Male Mean (Median)	Female Mean (Median)
Volume Day (ml)		1267 (1105)	1261 (1126)
Volume Night (ml)		446 (408)	468 (414)
Frequency Day		6.1 (6.0)	6.7 (6.5)
Frequency Night		0.4 (0.3)	0.4 (0.3)
Bladder Capacity Day		250 (234)	229 (220)
Bladder Capacity Night		334 (309)	332 (294)
24hr Volume	1730 (1576)	1713 (1512) *	1729 (1619)*
24hr Frequency	7.1 (7.0)	6.5 (6.3) *	7.1 (6.8) *

\* Extrapolated from references 4 and 5

## References

1. de Boer TA, Salvatore S, Cardozo L, et al. Pelvic organ prolapse and overactive bladder. *Neurourol Urodyn.* 2010;29(1):30-9.
2. Baden WE, Walker TA, Lindsay HJ. The Vaginal Profile. *Tex Med J.* 1968;64:56-8.
3. Blaivas JG, Panagopoulos G, Weiss JP, et al. The urgency perception score: validation and test-retest. *J Urol.* 2007;177(1):199-202.
4. Parsons M, Amundsen CL, Cardozo L, et al. Bladder diary patterns in detrusor overactivity and urodynamic stress incontinence. *Neurourol Urodyn.* 2007;26(6):800-6.
5. Amundsen CL, Parsons M, Tissot B, et al. Bladder diary measurements in asymptomatic females: functional bladder capacity, frequency, and 24-hr volume. *Neurourol Urodyn.* 2007;26(3):341-9.

# Non-Pharmacologic Treatment

## Treatment overview

- In general OAB is not cured, but patients often experience a reduction in symptoms and an improvement in quality of life.
- The three basic components to the treatment of OAB are:
  - Treatment of remediable conditions
  - Behavioral therapy
  - Pharmacotherapy (see next section)
- All patients should be educated about bladder function, fluid and dietary management, timed or prophylactic voiding, bladder training regimens, keeping a bladder diary, and pelvic floor exercises.

## Treatment of remediable conditions

- Health care providers should screen women with possible OAB for remediable conditions, including:<sup>1</sup>
  - Uro-gynecologic conditions
    - Pelvic organ prolapse
    - Stress incontinence
    - Urethral diverticulum
    - Bladder and ureteral stones
    - Bladder cancer
  - General medical conditions
    - UTI
    - Polyuria/polydipsia
    - Diabetes
    - Congestive heart failure
    - Medications

## Behavioral therapy for OAB

- Behavioral therapy has been shown to reduce incontinence episodes in patients with OAB by 57 percent and to reduce the quantity of urine loss by 54 percent.<sup>2,3</sup> Up to 15 percent of patients experience complete resolution of OAB symptoms with behavioral therapy alone, and half of all patients experience a substantial reduction in symptoms of 50 to 75 percent.<sup>2,3</sup>
- The components of behavioral therapy include bladder retraining, use of a bladder diary, lifestyle changes, and strategies to control urgency.



## Bladder retraining

- Bladder retraining, which increases bladder capacity and thus reduces OAB symptoms, is a cornerstone of behavioral therapy for OAB.
- Components of bladder retraining include:
  - Scheduled voiding regimen with gradually progressive voiding intervals
  - Urgency control strategies
  - Self-monitoring of voiding behavior (e.g., use of a bladder diary)
  - Positive reinforcement by health care provider
- Research has shown that bladder retraining can reduce incontinence by 50 to 87 percent.<sup>4</sup>

- Bladder retraining can be as effective as medication for urge incontinence.
- Bladder retraining with pelvic muscle rehabilitation is probably better than retraining alone.

### Use of a bladder diary

- A bladder diary can be a valuable tool for treating OAB as well as for evaluating the condition. (See the section on Diagnosis for more information.)
- By tracking their voiding habit, patients may recognize the cause of their symptoms by their pattern of voiding.
- Patients may be able to gradually increase the interval between voids or make lifestyle changes that reduce bladder symptoms.

### Lifestyle changes

- Several lifestyle changes can help reduce OAB symptoms. Health care providers can advise patients to:
  - Avoid dietary bladder irritants (e.g., alcohol, caffeine, tomatoes, citrus)
  - Moderate fluid intake
  - Improve their mobility
  - Address coexisting health issues
  - Improve bowel habits and regularity (e.g., increase fiber intake)

### Strategies to control urge

- Providers can encourage patients to adopt strategies to control urgency by relaxing and selectively contracting appropriate pelvic muscles (i.e., Kegel exercises), rather than rushing to the toilet when they feel the urge to urinate.
- Kegel exercises also can strengthen pelvic floor muscles (see Resources for Patients section for instructions).
- Providers can teach patients to control urgency with the following instructions:

- Anticipate those activities that bring on symptoms.
- Contract pelvic muscles quickly.
- Wait until the urge subsides; do not rush to the bathroom, instead stop and stay still for a few moments.
- Concentrate on suppressing the urge.
- Walk to the bathroom at a normal pace.

### Limitations of behavioral therapies

- Although successful in the majority of patients, behavioral therapy has limitations.
- Behavioral therapy requires a skilled and trained provider plus motivation and adherence in both the patient and the caregiver.
- Success depends on the intensity of the program.
- Behavioral therapy is expensive in terms of caregiver labor and time in certain settings (e.g., primary care, nursing home).

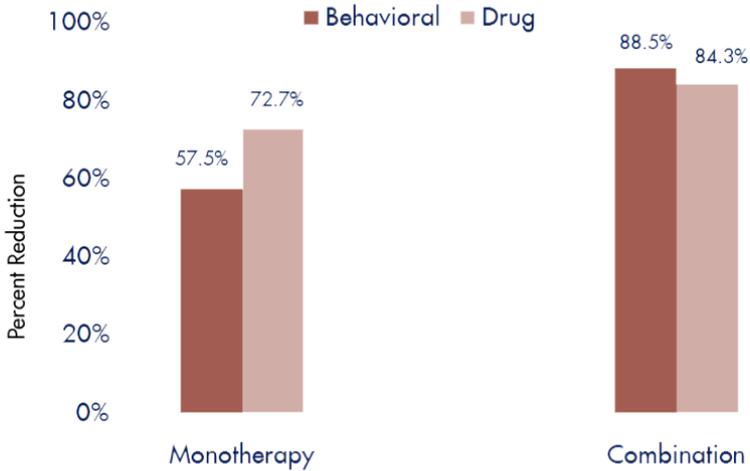
### References

1. Rosenberg MT, Newman DK, Tallman CT, Page SA. Overactive bladder: recognition requires vigilance for symptoms. *Cleve Clin J Med.* 2007;74(Suppl 3):S21-9.
2. Hanno PM, Wein A, Malkowicz SB, editors. *Clinical Manual of Urology, 3rd ed.* New York, NY : McGraw-Hill Professional Publishing; 2001.
3. Walsh PC, Retik AB, Vaughan ED, Wein AJ, editors. *Campbell's Urology, 8th ed.* Philadelphia: WB Saunders Company; 2002.
4. Burgio KL, Goode PS, Locher JL, et al. Behavioral training with and without biofeedback in the treatment of urge incontinence in older women: a randomized controlled trial. *JAMA.* 2002;288(18):2293-9.

## Pharmacologic Treatment

- Pharmacologic treatment can be combined with non-pharmacologic therapy.
- Combined treatment with behavior modification and antimuscarinics has been shown to be more efficacious than either modality used alone.<sup>1</sup>

Figure 2: Combination therapy reduction in incontinence<sup>1</sup>



## Combination Therapy Reduction in Incontinence<sup>1</sup>

- When non-pharmacologic and pharmacologic treatments fail, specialists can try other methods for treating OAB, such as botulinum toxin injections, neuromodulation, and surgery. These therapeutic modalities are not discussed in detail in this *Quick Reference Guide*.

## Pharmacologic therapies

- Four types of pharmacologic therapy are used to treat OAB:
  - Estrogen
  - Antimuscarinic drugs
    - Non-selective
    - Selective

- Tricyclic antidepressants
- Botulinum toxin (BOTOX®) injections

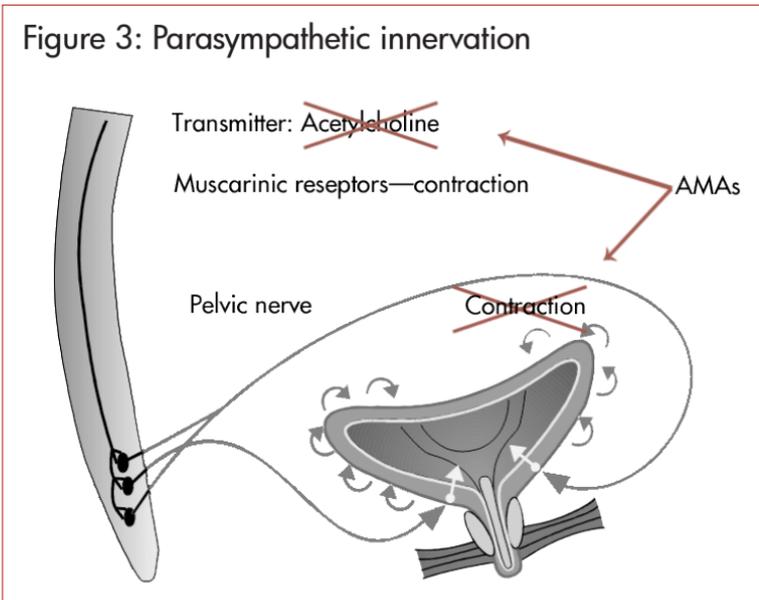
## Estrogen

- Local estrogen use is associated with overall subjective improvement in individuals with incontinence—fewer voids in 24 hours, fewer nocturnal voids, and less frequency and urgency.<sup>2</sup>
- However, systemic estrogen therapy may worsen incontinence.<sup>2,3</sup>

## Antimuscarinic drugs

- The mainstays of medical treatment for OAB are the antimuscarinic agents, also referred to as anticholinergic drugs.
- Antimuscarinic drugs inhibit involuntary detrusor contractions and thus reduce urgency (see sidebar).

## Parasympathetic innervation



- Available antimuscarinic agents have similar efficacy and safety profiles.

- The most important differences among these drugs relate to their side effects and tolerability.
- Individual agents vary based on receptor selectivity and serum concentration of the active drug.
- These agents can be divided into two basic groups:
  - Non-selective—have affinity for all muscarinic receptors
  - Selective—have relatively more affinity for M2 and M3 muscarinic receptors (see *The Role of Muscarinic Receptors in OAB Pharmacologic Treatment*)

### The Role of Muscarinic Receptors in OAB Pharmacologic Treatment

The primary neurotransmitter located at nerve endings on the detrusor muscle of the bladder is acetylcholine. Acetylcholine stimulates muscarinic nerve endings, of which there are five subtypes, named M1 through M5. Only M2 and M3 are highly concentrated in the bladder. M2 is more prevalent, but the M3 receptors are responsible for detrusor contraction.

Antimuscarinic drugs block the parasympathetic muscarinic receptors and appear to exert their effects on OAB through M2 and M3 receptors by inhibiting involuntary detrusor contractions. The effects on these and other muscarinic receptors are responsible for the side effects associated with these agents.

**Table 3. Side effects associated with receptor stimulation<sup>4-6</sup>**

Muscarinic receptor subtype	Side effects
M1	Impaired memory and cognition
M2	Prolongation of the QT interval, which can result in cardiac arrhythmias and tachycardia
M3	Dry mouth, constipation, blurred vision
M4	Impaired cognition
M5	Receptor present in the hippocampus and other areas of the brain, but stimulation-impaired cognition does not appear to be associated with M5 stimulation

Table 4. Available antimuscarinic agents

Medication	Dose	Receptor Affinity	Metabolism	Side Effects		
				Dry mouth	Constipation	CNS
Oxybutynin IR	5mg TID	M1, M2, M3, M4	Hepatic	*	*	*
Oxybutynin ER	4mg QD	M1, M2, M3, M4	Hepatic	**	**	*
Oxybutynin patch	3.9mg BIW	M1, M2, M3, M4	Hepatic, 2nd pass	***	***	**
Oxybutynin Gel	1 gm QD	M1, M2, M3, M4	Hepatic, 2nd pass	***	***	**
Tolterodine IA	4mg QD	M1, M2, M3, M5	Hepatic	**	***	**
Trospium	20 mg BID	M1, M2, M3, M4, M5	Renal	***	*	***
Solifenacin	5/10mg QD	M3	Hepatic	**	*	***
Darifenacin	7.5/15 mg	M3	Hepatic	**	*	***
Fesoterodine	4/8 mg QD	M1, M2, M3, M5	Hepatic	*	**	**

NOTE: \* denotes least severe, \*\* somewhat severe, and \*\*\* most severe  
Table used with permission from Jerry G. Blaivas, MD

## Oxybutynin (Ditropan®)

- First drug used for OAB
- Approved 1975
- Non-selective antimuscarinic agent
- Extensive first-pass metabolism
- Formulations:
  - Immediate release (IR) (Ditropan®)
    - Tabs: 5mg BID or TID; syrup 5mg/5ml
    - Onset 30-60 min, peak effects 3–6 hrs
    - Start at lower dose, increase gradually after 7 days
    - Max dose 30mg/day
  - Extended release (ER) (Ditropan® XL)
    - Tabs: 5mg, 10mg, 15mg QD
    - Better compliance, possibly fewer side effects
  - Transdermal (Oxytrol®)
    - 3.9mg/day 2x/wk
  - Gelnique®
    - Bypasses first-pass metabolism

## Tolterodine (Detrol®)

- Competitive muscarinic antagonist
- More effective than placebo in relieving frequency, urgency, and urge incontinence in patients with OAB<sup>7</sup>
- No effect on cognition compared with placebo
- Formulations:
  - Immediate release (Detrol®)
    - Tabs: 1 mg, 2mg BID
  - Extended release (Detrol® LA)
    - Tabs: 2mg, 4mg QD
    - Half-life 3 hrs

## Summary: Oxybutynin versus Tolterodine

- Both are equally effective at reducing urgency and urge incontinence.
- Oxybutynin may be superior at decreasing frequency but is more commonly associated with dry mouth.<sup>8</sup>
- Discontinuation rates are similar.
- Both have adherence issues due to side effects.
- Both improve quality of life.
- No head-to-head trials have been conducted that compare the agents' effect on quality of life.

## Trospium chloride (Sanctura<sup>®</sup>)

- Peripheral, non-selective antimuscarinic agent
- Does not cross blood-brain barrier
- Potentially low CNS side effects
- No cytochrome P450 metabolism
- Perhaps fewer drug-to-drug interactions
- Formulations:
  - Sanctura<sup>®</sup>
    - 20mg BID on empty stomach
  - Sanctura XR<sup>®</sup>
    - 60mg QD on empty stomach
    - No head-to-head trials versus extended-release forms
    - Dose reduced to 20mg QD in elderly or in patients with renal impairment

## Solifenacin succinate (VESIcare<sup>®</sup>)

- Competitive muscarinic receptor antagonist
- More selective for M3 receptors
- Formulations:
  - Tabs: 5mg, 10mg QD

- Superior to placebo in reducing frequency, urgency, urge incontinence, and nocturia<sup>9,10</sup>
- No QT effect, so potentially safe with heart disease
- Superior to tolterodine IR 2mg BID in reducing urge and urge incontinence with less dry mouth<sup>11</sup>
- Superior to tolterodine ER 4mg in decreasing urge, urge incontinence, and pad use<sup>12</sup>

### Darifenacin (Enablex®)

- Bladder-selective M3 receptor antagonist
- Formulations:
  - Tabs: 7.5mg, 15mg QD
- Superior to placebo in reducing frequency, urgency, urge incontinence<sup>13</sup>
- Dry mouth and constipation more common than with placebo
- No differences in memory versus placebo and oxybutynin ER<sup>14,15</sup>
- High selectivity for the M3 receptor relative to the M1 receptor (9.3 times more affinity), which may minimize or avoid cognitive impairment<sup>16-18</sup>
- No alteration of QT interval
- Theoretically, risk of torsades de pointes is decreased; clinical relevance uncertain, potentially safe with heart disease
- No renal dosing necessary

### Fesoterodine fumarate (Toviaz™)

- Competitive muscarinic receptor antagonist
- Formulations:
  - Tabs: 4mg, 8mg QD
- Superior to placebo in reducing the number of urge incontinence episodes and micturitions per 24 hours
- No renal dosing in mild-moderate renal disease; avoid 8mg dose with severe renal disease

- No QT interval prolongation
- No comparative trials conducted

#### Summary: Cognitive side effects with antimuscarinic agents<sup>14</sup>

- Oxybutynin adversely affects cognition.
- Darifenacin, solifenacin, and tolterodine do not.
- Fesoterodine and trospium probably do not.

#### Tricyclic antidepressants

- Imipramine and amitriptyline are used.
- Both drugs inhibit uptake of norepinephrine and serotonin.
- Demonstrate anticholinergic and sympathomimetic (i.e., stimulation of sympathetic nervous system) effects.
- Suppress detrusor contractions and increase outlet resistance by urethral contraction; both of these mechanisms of action promote urinary incontinence but can also cause urinary retention.
- Effects are additive to those of antimuscarinic agents.
- Not approved by Food and Drug Administration for OAB and should not be used for primary treatment.
- Generally used in combination with antimuscarinic agents for patients with refractory OAB.

#### Guidance on drug selection

- All antimuscarinic agents have approximately the same efficacy and side effect profile.
- The incidence of side effects associated with a particular antimuscarinic agent varies based on:
  - Route of administration
  - Receptor specificity
  - Chemical structure
  - Metabolic breakdown pathways

- Generally, controlled-release medications are associated with fewer adverse events.
- If there is a concern about cognitive function, a selective M3 receptor blocker or one that does not have an affinity for crossing the blood-brain barrier is advisable.
- For patients who have pre-existing constipation, non-selective antimuscarinics are preferable to M3 selective blockers because of the presence of M3 receptors in the bowel.
- In patients with hepatic impairment, trospium or fesoterodine may be preferable because they are not processed by the CYP3a4 system. Avoid darifenacin in patients with severe hepatic impairment.
- Specific guidance:
  - Begin with either tolterodine or oxybutynin.
  - If the patient has cognitive issues, use darifenacin (caution in patients with constipation), tolterodine, or solifenacin.
  - Avoid in patients with hepatic impairment.
  - For second-line drugs, try non-generic agents.
  - If symptoms continue despite maximum dose of antimuscarinics for four weeks and the patient is tolerating the anticholinergic side effects, consider adding a tricyclic antidepressant. NOTE, however, that the side effects of this combination can be limiting.

## Specialty treatments for refractory OAB

- For patients with refractory OAB (i.e., no response to treatment for four to six weeks), referral to a specialist is prudent.
- Specialty treatments include injections of botulinum toxin, neuromodulation, enterocystoplasty, and urinary diversion.
  - Botulinum toxin
    - Injections into bladder
    - 40%–80% success, but requires repeated injections every 6 to 9 months<sup>19</sup>

- Relatively high incidence of temporary urinary retention requiring intermittent self-catheterization until the effects wear off
- Neuromodulation<sup>20</sup>
  - Implantable electrical stimulation device
  - 56%– 90% success (using a primary outcome measure of a 50% decrease in OAB symptoms at 6 months)
  - Complications are minor.
- Enterocystoplasty<sup>21-23</sup>
  - Major abdominal surgery: part of the intestine (the ileum or ileocecal segment) is detached from the rest of the bowel, reconfigured, and anastomosed to the bladder.
  - > 90% success
  - Afterward the patient may void normally, require intermittent self-catheterization, or wear an external appliance that collects the urine.
- Urinary diversion<sup>21</sup>
  - Major abdominal surgery: a continent abdominal stoma may be created for intermittent catheterization.
  - Appropriate for patients with disabilities that make catheterizing through the urethra impractical.
  - > 90% success

### Criteria for specialist referral

- Patients with OAB should be referred to urologic or gynecologic specialists under the following circumstances:
  - Hematuria
  - Unclear diagnosis
  - Presence of voiding symptoms
  - Presence of pelvic organ prolapse
  - No response to therapy

- Elevated post-void residual
- Previous pelvic surgery
- Bladder pain
- Presence of neurologic disease

## References

1. Burgio KL, Locher JL, Goode PS. Combined behavioral and drug therapy for urge incontinence in older women. *J Am Geriatr Soc.* 2000;48(4):370-4.
2. Cody JD, Richardson K, Moehrer B, et al. Oestrogen therapy for urinary incontinence in post-menopausal women. *Cochrane Database Syst Rev.* 2009;(4):CD001405.
3. Hendrix SL, Cochrane BB, Nygaard IE, et al. Effects of estrogen with and without progestin on urinary incontinence. *JAMA.* 2005;293(8):935-48.
4. Hegde SS. Muscarinic receptors in the bladder: from basic research to therapeutics. *Br J Pharmacol.* 2006;147(Suppl 2):S80-7.
5. Kay GG, Ebinger U. Preserving cognitive function for patients with overactive bladder: evidence for a differential effect with darifenacin. *Int J Clin Pract.* 2008;62(11):1792-800.
6. Staskin DR, Zoltan E. Anticholinergics and central nervous system effects: are we confused? *Rev Urol.* 2007;9(4):191-6.
7. Appell RA. Clinical efficacy and safety of tolterodine in the treatment of overactive bladder: a pooled analysis. *Urology.* 1997; 50(Suppl 6A):90-6.
8. Diokno AC, Appell RA, Sand PK, et al.; OPERA Study Group. Prospective, randomized, double-blind study of the efficacy and tolerability of the extended-release formulations of oxybutynin and tolterodine for overactive bladder: results of the OPERA trial. *Mayo Clin Proc.* 2003;78(6):687-95.
9. Cardozo L, Castro-Diaz D, Gittelman M, et al. Reductions in overactive bladder-related incontinence from pooled analysis of phase III trials evaluating treatment with solifenacin. *Int Urogynecol J Pelvic Floor Dysfunct.* 2006;17(5):512-9.
10. Brubaker L, FitzGerald MP. Nocturnal polyuria and nocturia relief in patients treated with solifenacin for overactive bladder symptoms. *Int Urogynecol J Pelvic Floor Dysfunct.* 2007;18(7):737-41.
11. Chapple CR, Rechberger T, Al-Shukri S, et al.; YM-905 Study Group. Randomized, double-blind placebo- and tolterodine-controlled trial of the once-daily antimuscarinic agent solifenacin in patients with symptomatic overactive bladder. *BJU Int.* 2004;93(3):303-10.
12. Chapple C, Khullar V, Gabriel Z, Dooley JA. The effects of antimuscarinic treatments in overactive bladder: a systematic review and meta-analysis. *Eur Urol.* 2005;48(1):5-26.
13. Haab F, Stewart L, Dwyer P. Darifenacin, an M3 selective receptor antagonist, is an effective and well-tolerated once-daily treatment for overactive bladder. *Eur Urol.* 2004;45(4):420-9.
14. Lipton RB, Kolodner K, Wesnes K. Assessment of cognitive function of the elderly population: effects of darifenacin. *J Urol.* 2005;173(2):493-8.

15. Kay G, Crook T, Rekeda L, et al. Differential effects of the antimuscarinic agents darifenacin and oxybutynin ER on memory in older subjects. *Eur Urol.* 2006;50(2):317–26.
16. Napier C, Gupta P. Darifenacin is selective for the human recombinant M3 receptor subtype. *Neurourol Urodyn.* 2002;21:A445. (abstract)
17. Kay GG, Wesnes KA. Pharmacodynamic effects of darifenacin, a muscarinic M3 selective receptor antagonist for the treatment of overactive bladder, in healthy volunteers. *BJU International.* 2005;96(7):1055–62.
18. Wesnes K, Lipton R, Kolodner K, Edgar C. Darifenacin, an M3 selective receptor antagonist for the treatment of overactive bladder, does not affect cognitive function in elderly volunteers. *Eur Urol.* 2004;3(2):131. (abstract)
19. Karsenty G, Denys P, Amarenco G, De Seze M, Gamé X, Haab F, et al. Botulinum toxin A (Botox) intradetrusor injections in adults with neurogenic detrusor overactivity/neurogenic overactive bladder: a systematic literature review. *Eur Urol.* 2008;53(2):275–87.
20. Chartier-Kastler E. Sacral neuromodulation for treating the symptoms of overactive bladder syndrome and non-obstructive urinary retention: >10 years of clinical experience. *BJU Int.* 2008;101(4):417–23.
21. Blaivas JG, Weiss JP, Desai P, et al. Long-term followup of augmentation enterocystoplasty and continent diversion in patients with benign disease. *J Urol.* 2005;173(5):1631–4;
22. Flood HD, Malhotra SJ, O'Connell HE, et al. Long-term results and complications using augmentation cystoplasty in reconstructive urology. *Neurourol Urodynam.* 1995;14(4):297–309.
23. Herschorn S, Hewitt RJ. Patient perspective of long term outcome of augmentation cystoplasty for neurogenic bladder. *Urology.* 1998;52(4):672–8.

## Counseling Tips

### Screening for OAB

- Use these questions to screen patients for OAB:
  - Do you ever feel a compelling urge to urinate that is difficult to defer?
  - Do you ever leak urine? Under what circumstances?
  - How often do you urinate in 24 hours?
  - How many times do you get up to urinate at night?

### Assessing the effects of OAB

- Use these questions to assess the effects of OAB on the patient's quality of life:
  - Do symptoms such as an urgent need to urinate, frequent urination, or leaking of urine affect your ability to:
    - Socialize?
    - Travel?
    - Fulfill your occupational or personal roles?
    - Be sexually active?
  - Do your symptoms limit your ability to participate in or attend activities and events outside the home?
  - Do you ever experience embarrassment because of your symptoms?
  - Has anyone expressed concern about your symptoms?

### Educating patients

- Educate patients about:
  - Bladder function
  - Fluid and dietary management
  - Timed or prophylactic voiding
  - Bladder training regimens

- Keeping a bladder diary
- Pelvic floor exercises
- Refer patients to educational materials (see Resources for Patients section).

## Supporting lifestyle changes

- Advise patients to:
  - Avoid dietary bladder irritants (e.g., alcohol, caffeine, tomatoes, citrus).
  - Moderate fluid intake.
  - Improve their mobility.
  - Address coexisting health issues.
  - Improve bowel habits and regularity (e.g., increase fiber intake).
- Enlist caregiver's support, as appropriate.

## Exploring treatment options

- Explore available options with patients.
- Explain the options for non-pharmacologic and pharmacologic therapy.
- Discuss potential drug-related side effects and methods for minimizing or avoiding them.
- Discuss the timing of referral to a urologist or gynecologic specialist for treatment.
- Encourage patients to ask questions and seek additional sources of information and support.

## Referring for specialist's care

- Refer to a specialist patients with:
  - Hematuria
  - Unclear diagnosis
  - Presence of voiding symptoms

- Presence of pelvic organ prolapse
- No response to therapy
- Elevated post-void residual
- Previous pelvic surgery
- Bladder pain

## Resources for Patients

### Patient education materials

#### **American Academy of Family Physicians**

Patient education materials on urinary incontinence  
[www.aafp.org/afp/20001201/2447ph.html](http://www.aafp.org/afp/20001201/2447ph.html)

#### **Mayo Clinic**

Patient education materials on OAB  
[www.mayoclinic.com/health/overactive-bladder/DS00827](http://www.mayoclinic.com/health/overactive-bladder/DS00827)

#### **American Geriatric Association, AGS Foundation for Health in Aging**

Patient education materials on urinary incontinence  
[www.healthinaging.org/public\\_education/pef/urinary\\_incontinence.php](http://www.healthinaging.org/public_education/pef/urinary_incontinence.php)

#### **American Urological Association**

Patient education materials on OAB  
[www.urologyhealth.org/adult/index.cfm?cat=03&topic=450](http://www.urologyhealth.org/adult/index.cfm?cat=03&topic=450)

#### **National Association for Continence**

Patient education materials on urinary incontinence  
[www.nafc.org/bladder-bowel-health](http://www.nafc.org/bladder-bowel-health)

#### **National Institutes of Health**

Patient education materials on urinary incontinence  
[www.nlm.nih.gov/medlineplus/urinaryincontinence.html](http://www.nlm.nih.gov/medlineplus/urinaryincontinence.html)

### Patient exercise instructions

#### **American Academy of Family Physicians**

Patient instructions for pelvic muscle exercise  
[www.aafp.org/afp/20001201/2452ph.html](http://www.aafp.org/afp/20001201/2452ph.html)

### Sample bladder diary

#### **National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health**

Bladder diary for download  
<http://kidney.niddk.nih.gov/kudiseases/pubs/diary>



Association of  
Reproductive  
Health  
Professionals

Providing evidence-based education to health care professionals and their patients since 1963.

Want more? ARHP's evidence-based, peer-reviewed materials are available to providers at no cost. To request printed copies, contact [publications@arhp.org](mailto:publications@arhp.org) or (202) 466-3825 or download this guide at [www.arhp.org/guide](http://www.arhp.org/guide).