

New Treatments in Overactive Bladder and Implications for Managed Care

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Summary

Overactive bladder (OAB) is a significant social, medical, and cost issue for a large percentage of the population and these problems only increase as one ages. Current treatment with behavior management and anticholinergic medications does not significantly improve bladder capacity, or improve continence. Newer treatments, such as neurostimulation with implanted devices and injection of the bladder muscles with botulinum toxin, indicate that such interventions improve these parameters to a greater extent.

Key Points

- OAB is a significant problem both from a quality-of-life and a cost perspective.
- Oral medications and behavior therapies that are currently available do not optimally control the disease.
- The ultimate goal with OAB is to improve quality of life by decreasing symptoms and achieving continence.
- Neurostimulation with implanted devices or injected botulinum toxin appears to result in improvements in continence rates and bladder capacity.

ACCORDING TO THE International Continence Society, overactive bladder is a symptom syndrome of urgency, with or without urge incontinence, usually with frequency and nocturia.¹ Overactive bladder really incorporates a variety of issues including frequency, nocturia, urgency, and incontinence. Frequency is defined as voiding more than eight times a day. Nocturia is having to get up more than two times at night. Urgency is a sudden, compelling desire to urinate. Incontinence is often the result of urgency. Incontinence causes much of the patient distress and difficulty related to OAB.

In differentiating the type of urinary incontinence (UI), there is overlap of the symptoms between urge UI and stress UI. Stress incontinence is urine leakage during some type of activity, such as coughing or sneezing. Stress incontinence is a structural problem with the urethra. Any type of increased abdominal exertion, whether a cough or strain or sneeze, puts increased abdominal pressure on top of the bladder, which overcomes the resistance of the urethra. The patient will leak a defined amount of urine at a defined

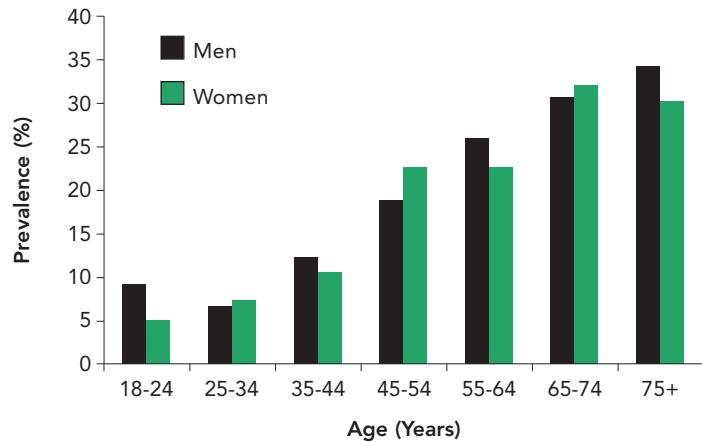
moment. In differentiating stress incontinence from urge incontinence secondary to OAB, the issue with OAB is a spasticity of the bladder muscle that will suddenly cause a contraction and leakage of urine. Typically, the leakage of urine that occurs is a large volume loss. The key component in OAB is dealing with the bladder hypersensitivity and spasticity to decrease symptoms and prevent incontinence. OAB can occur with pelvic prolapse, urinary tract infection, and benign prostatic hyperplasia. The bottom line is that stress incontinence is a urethral problem, whereas OAB is a bladder problem.

Almost 16 percent of the U.S. population, approximately 33 million Americans, will have symptoms of OAB (see Exhibit 1).² One third of people with OAB symptoms will have accompanying urge incontinence. Prevalence of OAB increases with age. Interestingly, men have nearly equal prevalence as women. Roughly 10 percent of people in their 30s will have symptoms of OAB, whereas 30 percent of people in their 60s will have symptoms of OAB.

OAB has a significant impact on a person's lifestyle

Exhibit 1: Prevalence Increases with Age²

- Overall, 16.6% had symptoms of OAB
- Prevalence of OAB increases with age
- Prevalence similar in men and women
- Other risk factors
 - > neurological disease
 - > bladder outlet obstruction
 - > stress incontinence



(see Exhibit 2).³ It affects all quality-of-life domains including social, sexual, work environment, and others. Patients with OAB also can become withdrawn from society and depressed.⁴

Pathophysiology

The bladder is a simple organ for urine storage and elimination, but it has a complex neuroanatomy. The control center for the bladder is at the base of the brain. Parasympathetic, sympathetic, and somatic nerves innervate the bladder, the stem of the bladder and the pelvic floor. With normal micturition, as the bladder starts filling, stress receptors are triggered within the bladder. The stress receptors will then signal the sacral micturition center, causing the bladder to contract reflexively, the urethra to relax, and urination to occur. As children mature, they gain cognitive control of urination. Parasympathetic input from the central nervous system inhibits bladder contraction and tightens the urethral area.

The neurogenic theory of OAB proposes that several things can disrupt normal bladder activity and lead to OAB. Decreased central inhibitory control that stems from brain injury, stroke, multiple sclerosis, and spinal cord injury can lead to OAB. Additionally, the receptors that are within the bladder can have hypersensitivity. The nerve impulses that come from the bladder as it is stretching can be hypersensitive and actually cause more afferent stimulation.

Treatment

The traditional approach to OAB treatment includes a combination of behavioral therapy and pharmacologic therapy. Currently, surgical therapy is rarely done.

Behavioral therapy is the foundation for OAB treatment. This entails bladder training, dietary modification, patient education, scheduled voiding,

Exhibit 2: OAB—Personal and Societal Burden^{3,4}

- Increased hospitalization costs (\$49.1 million/year)³
- Increased nursing home stays (\$1.47 billion/year)³
- Frequent occurrence of urinary tract infections (\$1.19 billion/year)³
- Increased risk for falls and fractures (\$306.9 million/year)³
- Frequent occurrence of skin irritation (\$38.4 million/year)³
- 60% of OAB patients suffer from depression²

and positive reinforcement. Additional behavior interventions include pelvic floor exercises, biofeedback, and electric stimulation therapy. For behavioral therapy to be successful, an extremely motivated and dedicated patient is required. On the positive side, with behavioral therapy, continence rates of up to 30 percent can be achieved and most people will have some improvement in symptoms. The negative issues include difficulty in sustaining patient motivation and a lack of reimbursement to the health professional providing training.

The most common aspect of treatment is pharmacotherapy, with numerous medications recently marketed for OAB. However, medications have not significantly improved continence rates over behavior therapy alone. The medications result in about a 30 percent continence rate. Additionally, the side effects of dry mouth, constipation, blurred vision, and confusion are a limiting factor for these medications. When prescription claims data are examined, about 80 percent of people are discontinuing medication management

Exhibit 3: Neuromodulation for OAB

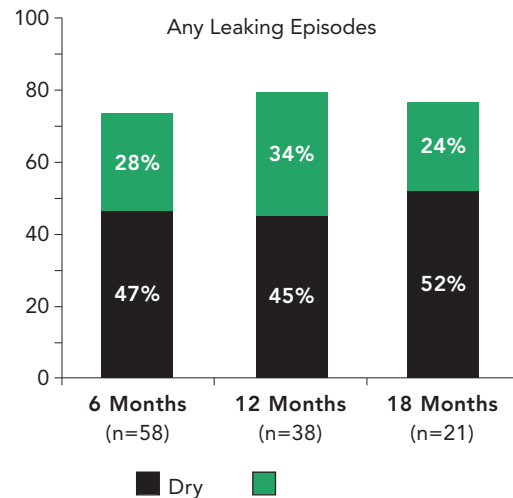


within three months primarily due to lack of efficacy, in addition to intolerable side effects, or a combination of both. Therefore, OAB is not ideally managed with currently available pharmacologic therapy.

New treatments for OAB are in the realm of neuromodulation. Neuromodulation is trying to alter the natural pathways of the nervous system. There are three main neuromodulation systems available or under study: sacral nerve root stimulation, posterior tibial stimulation, and pudendal nerve stimulation (see Exhibit 3). All of these therapies are targeting the spinal cord and altering the natural nerve reflex pathways to the bladder. The first therapy approved was InterStim, which is sacral nerve modulation. InterStim is FDA approved for urinary urgency frequency, urge incontinence, and urinary retention. This therapy requires a test phase to determine if the therapy will work and, if it will, surgical implantation of the stimulation device. To move on to the implant phase, the patient should have at least a 50 percent improvement in urge incontinence. The benefit to sacral neuromodulation therapy is longstanding results of 47 to 50 percent continence rate compared with a 30 percent rate with behavioral or medication therapy (see Exhibit 4).⁵

Another neuromodulation device that is being tested is tibial nerve stimulation. This is an office-based therapy that stimulates the tibial nerve for about 20 to 25 minutes once a week for three months. A small acupuncture needle is placed into the tibial nerve. The needle is connected to an external battery generator and a grounding pad. When a therapy session is complete, the acupuncture needle is removed. In a small sample of 53 patients treated over a 12-week period, there was a 25 percent reduction in urinary frequency, a 21 percent reduction in nocturia, and a 35 percent reduction in incontinence.⁶ To achieve continence, tibial nerve stimulation may not be significantly better than pharmacotherapy or behavior management. It may be an option for patients who do

Exhibit 4: Urge Incontinence Sustained Clinical Efficacy



not want to proceed to the implantable therapies. A future improvement of tibial nerve neuromodulation will be a small implantable device so patients will have the ability to do the therapy at home.

A third neuromodulation device under study stimulates the pudendal nerve. The theoretical basis of this device is that stimulation of the pudendal nerve results in increased afferent sensation to the sacral two, three, and four nerve roots. Stimulation of the third sacral nerve has been shown to be effective in treating voiding dysfunction. The stimulation device is known as a bion, which is a small single-channel, self-powered, implantable pulse generator with integrated electrode. It is implanted next to the pudendal nerve (see Exhibit 3). To determine if the device is likely to work, a test phase must be conducted. In the physician's office under local anesthesia, a small stimulating electrode is placed at the patient's pudendal nerve to stimulate the nerve for 15 minutes. Bladder volume is tested before and after the stimulation. If the patient has a greater

than 50 percent increase in bladder volume, a greater than 50 percent increase in first sensation to void, or an increase of 50 percent from the first involuntary bladder contraction, he or she would be a candidate to have the small device implanted. Unlike the InterStim device, the bion has to be recharged using a base station in a chair pad. The patient sits on this chair pad for 15 minutes a day for recharging.

In one published study of 14 subjects treated with pudendal stimulation, only six subjects passed the stimulation test.⁷ Of six patients who proceeded to the implant, there were some reductions in urge incontinence, and bladder volume increased by 120 to 130 cubic centimeters. Bladder capacity is a key component that drives frequency. The available pharmacologic agents only increase bladder capacity by 30 cubic centimeters.

Another area of research is biological neuromodulation, which uses botulinum toxin. Botulinum toxin, derived from *Clostridium botulinum*, inhibits the release of acetylcholine from the nerve terminal and blocks smooth muscle contraction. Although other types are available, botulinum toxin A (Botox) is the type primarily under investigation for OAB. For OAB, the botulinum toxin is injected into the detrusor muscle of the bladder via a cystoscope. The procedure can be office or hospital based, depending on the practitioner.

A benefit of botulinum toxin in treating OAB is that it is not permanent. Its effects are temporary, typically lasting six to nine months for smooth muscles like the detrusor. Although not FDA approved for the indication, botulinum toxin has been used for several years for bladder and urinary tract issues. It has been used for neurogenic overactivity, bladder pain of interstitial cystitis, non-neurogenic overactivity, outflow obstruction secondary to BPH, and detrusor-sphincter dyssynergia.

Several peer-reviewed studies of botulinum toxin in the treatment of OAB have been published. The

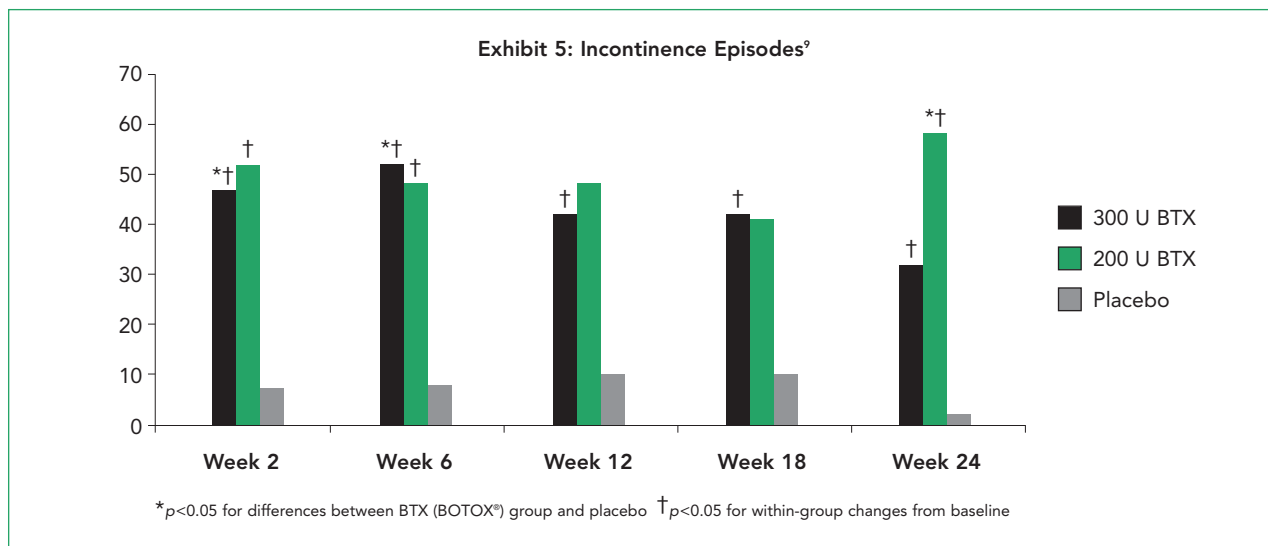
majority of published studies have been for neurogenic OAB. One multi-center trial of 200 patients showed a greater than 50 percent improvement in bladder capacity.⁸ A multi-center trial of patients with multiple sclerosis or spinal cord injury who had leaking of urine between intermittent catheterization treated with botulinum toxin A was published in the *Journal of Urology* in 2005.⁹ The injections resulted in a 45 to 50 percent reduction in incontinence two weeks after injection (see Exhibit 5). Bladder capacity improved significantly (see Exhibit 6). Statistical improvements in quality of life measures were seen as early as two weeks after the injections. Quality of life continued to improve all the way to week 24. There were no adverse events that were attributed to the botulinum toxin therapy.

In rare instances, injection of botulinum toxin B into the bladder has been reported to cause transient generalized weakness, but this has not been reported with the type A toxin.¹⁰ Urinary retention also is a possible side effect. At this time, there has been no evidence of long-term structural bladder change caused by toxin injections.¹¹

More study is needed to determine the ideal dose, number of injections, and injection technique. Another issue to be addressed is pharmacoeconomics analyses comparing botulinum toxin to other therapies.

Managed Care Issues

In addition to being a quality-of-life issue, OAB is also a cost issue. An example of these costs comes from SelectHealth, formerly InterMountain Health. SelectHealth is a commercial health plan covering a young population of 480,000 in Utah and Idaho. The group examined its claims data for OAB costs for 2005 (see Exhibit 7). Overall, its costs for OAB medications were 18 cents per member per month. The health plan



also found that patients were not regularly filling their OAB medication prescriptions and frequently were switched from one medication to another. When medical claims costs were considered, the health plan spent \$3.2 million for people with OAB, or 58 cents per member per month. Neurostimulation, while infrequently used in this health plan, was expensive. Ten claims for seven members resulted in \$8,500 in costs. Although these costs are only \$0.01 per member per month, it's important to note that the costs were generated by only 10 claims. The plan's estimated total per member per month cost for all care related to OAB was \$0.79, which was significant. In managed care finances, 25 cents per member per month attracts attention. Thus, OAB is not an insignificant problem for a commercial HMO. Health plans with a large elderly population would have even higher costs.

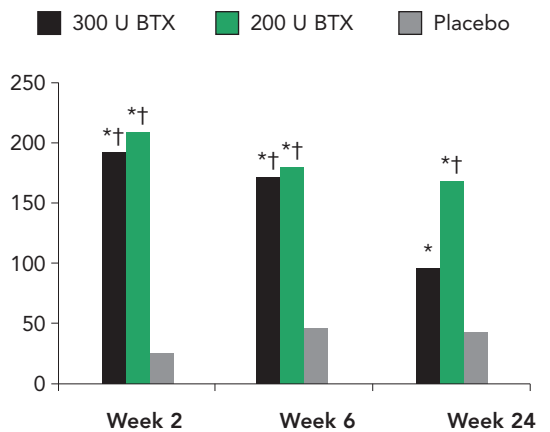
Conclusion

Because behavior and medication therapies are not meeting the needs of many patients, neuromodulation and botulinum toxin are likely future therapies for OAB. These therapies do not require patient motivation to be effective and avoid the typical adverse effects of oral medications. Overall, therapy most likely will employ a combination of approaches to significantly improve patients' quality of life. **JMCM**

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Exhibit 6: Maximum Cystometric Capacity⁹



* $p < 0.05$ for within-group changes from baseline

† $p < 0.05$ for pairwise contrasts between BTX (BOTOX[®]) groups versus placebo

Exhibit 7: Cost Implications of OAB for MCOs SelectHealth Example

Claims for OAB

- 476,000 total members in 2005
- 5,033 members with claims for OAB
- 4,173 members with physician claims
- 1,511 members with outpatient facility claims
- 316 members with OAB and claims for UTIs
- 195 members underwent surgery for OAB
- 7 members underwent sacral nerve stimulation

Cost to the Health Plan

- Total medication costs (including patient co-pays): \$1,025,795.69 (\$0.18 PMPM)
- Total procedure/physician fee/ancillary costs: \$3,296,263.34 (\$0.58 PMPM)
- Total neurostimulation procedure costs: \$85,927.99 (\$0.015 PMPM)
- Total office/lab costs related to treating infections secondary to OAB: \$92,131.02 (\$0.16 PMPM)*
- Overall PMPM Costs: \$0.79

OAB = over active bladder; UTI = urinary tract infection; PMPM = per member per month

*Antibiotic costs specifically for treating infections secondary to OAB not available.

Faculty

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Disclosure

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Dr. Schaecher has no real or perceived financial relationships that present a conflict of interest.

Accreditation

The National Association of Managed Care Physicians (NAMCP) is accredited by the Accreditation Council for Continuing Medical

Education to sponsor continuing medical education for physicians. NAMCP designates this activity for a maximum of 1 *AMA PRA Category I credits™*. Each physician should claim credit commensurate with the extent of their participation in the activity.

The American Association of Managed Care Nurses (AAMCN) has been approved as a provider of continuing education by the Virginia Nurses Association (VNA) for the period of Jan. 1, 2004, to Dec. 31, 2006. VNA is accredited as an approver of continuing education in nursing by the American Nurses Credentialing Center's Commission on Accreditation. Nurses who complete this activity will be awarded 1.2 contact hours.

This activity has been approved by the American Board of Managed Care Nursing for 1.2 contact hours toward CMCN recertification requirements.

This activity was held live at the NAMCP Spring Managed Care Forum. This activity is valid from Sept. 1 to Dec. 31, 2006.

POST TEST

INSTRUCTIONS

Read the article, answer the post test questions, complete the evaluation form, and submit to Ann Patrick either by fax 804-747-5316 or mail: 4435 Waterfront Drive, Suite 101, Glen Allen, VA 23060.

1. OAB is a symptom syndrome of urgency, with or without urge incontinence, usually with frequency and nocturia.

- a. True
- b. False

2. Today, 33 million adults have OAB, and this number includes men and women.

- a. True
- b. False

3. The burden of OAB includes:

- a. Requirement for specialized underwear and bedding
- b. Avoidance of sexual contact and intimacy
- c. Limitation or cessation of physical activities
- d. Reduction in social interaction
- e. Fear of being a burden and urine odor
- f. All of the above

4. The treatment cascade for OAB includes behavioral therapy, pharmacotherapy, and neuromodulation treatment.

- a. True
- b. False

5. Sacral nerve stimulation has indications for

- a. Urge incontinence
- b. Urgency and frequency
- c. Urinary retention
- d. All of the above

6. Tibial Nerve Stimulation reduces urge incontinence 35 percent.

- a. True
- b. False

7. In one trial, treatment with botulinum toxin showed a 50 percent increase in bladder capacity

- a. True
- b. False

8. Future direction for OAB treatment with botulinum toxin includes:

- a. Pharmacoeconomics of therapies
- b. Standardization of dosing
- c. Standardization of injection technique and number of injections
- d. All of the above

9. A managed care organization can spend up to \$0.79 per member per month on OAB claims.

- a. True
- b. False

10. New therapies for OAB most likely will be a combination of approaches to improve the patient's quality of life.

- a. True
- b. False

OAB ANSWER SHEET

There is only one correct answer per question.
Circle your answers clearly.

1. a b

2. a b

3. a b c d e f

4. a b

5. a b c d

6. a b

7. a b

8. a b c d

9. a b

10. a b

ACTIVITY EVALUATION

1. Please evaluate this activity based on the following scale:

4 Excellent 3 Good 2 Fair 1 Poor

Activity met my expectations

4 3 2 1

Activity was free of bias

4 3 2 1

Activity content was understandable

4 3 2 1

Presenters were free of bias

4 3 2 1

Method of learning was beneficial

4 3 2 1

I will change my practice patterns by (please specify):

My practice patterns will not change.

Name: _____

MD DO Other _____

Mailing Address: _____

City: _____

State: _____ ZIP: _____

Phone: _____

Fax: _____

E-mail: _____

Send my certificate by:

U.S Mail E-mail

I heard about this activity from:

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