Comparing Direct Medical Costs of OnabotulinumtoxinA With Other Common Overactive Bladder Interventions

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ABSTRACT

Objectives: To compare the estimated direct costs of onabotulinumtoxinA with other overactive bladder syndrome (OAB) interventions for patients inadequately managed by an anticholinergic.

Study Design: A cost analysis compared the direct annual costs of 12 common pharmaceutical treatments, including branded and generic anticholinergics, and mirabegron; 1 injection procedure (intravesical injection of onabotulinumtoxinA); and 2 devices (sacral nerve stimulation [SNS] device implantation and percutaneous tibial nerve stimulation [PTNS]).

Methods: Direct medical treatment costs were assessed from a United States payer perspective and included costs of drugs and/or procedures, administration (if applicable), and routine follow-up care. Drug acquisition costs were based on average wholesale price minus 15% and maximum allowable cost.

Results: During year 1, costs of pharmaceutical treatment ranged from $500 (oxybutynin) to $3472 (Detrol LA [long acting]); the cost for an injection procedure was $1892 (onabotulinumtoxinA); and costs for devices were $3395 (PTNS) and $19,443 (SNS). At years 5 and 10, respectively, costs were $2500 to $17,360 (oxybutynin) and $5000 to $34,720 (Detrol LA) for pharmaceutical treatments; $9458 to $18,916 for onabotulinumtoxinA; $11,849 to $21,316 for PTNS; and $21,316 to $33,801 for SNS.

Conclusions: This analysis suggests that short- and long-term costs of OAB treatment vary considerably. Pharmaceutical therapies were not necessarily less costly than injection procedures or devices. Among the injection procedure and device treatments, onabotulinumtoxinA was the least costly option at all time points. Although cost is an important component when comparing these treatments, aspects such as efficacy and safety must be considered when deciding on an appropriate treatment for OAB.

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The International Urogynecological Association and the International Continence Society define overactive bladder syndrome (OAB) as a constellation of urinary symptoms, characterized by urinary urgency, and usually accompanied by frequency and nocturia, in the absence of urinary tract infection (UTI) or other obvious pathology.[1] OAB may occur with or without urinary incontinence (UI). OAB is among the most common disorders among older adults, affecting approximately 16.0% of men and 16.9% of women in the United States.[2] The prevalence of OAB peaks around age 60 for both men and women; however, increasing age is associated with higher prevalence of OAB among men but not women.[3,4]

Owing to its high prevalence, OAB places a substantial cost burden on society and payers, in particular. The total societal cost of OAB with UI in the United States was projected to be $76.2 billion in 2015, and is expected to increase as the population ages.[5] The majority of the total cost of OAB (75%) is attributable to direct medical costs of treatment, such as pharmacotherapy or surgical procedures.

Much of the treatment cost is due to the need to try multiple agents or procedures. Although behavioral therapy, such as fluid restriction, or bladder or pelvic floor muscle training, are recommended as first-line therapy in OAB by the American Urological Association, most patients will require pharmacological treatment and are usually initiated on generic anticholinergic agents.[6] However, a retrospective claims analysis of 103,250 patients diagnosed with OAB who were prescribed an anticholinergic found that 92% of patients failed their anticholinergic treatment.[7] Published OAB patient surveys have described poor treatment efficacy and intolerable adverse effects (AEs) as the main reasons for anticholinergic discontinuation.[8,9] Patients who fail initially prescribed anticholinergic therapy still have a variety of treatment options. These include long-acting branded anticholinergics; topical anticholinergic formulations; beta-3 adrenergics, such as mirabegron; bladder chemodenervation with onabotulinumtoxinA injection; and implantable devices, such as sacral neuromodulation (ie, sacral nerve stimulation

PRACTICAL IMPLICATIONS

Real-world studies show that 92% of overactive bladder syndrome (OAB) patients fail first-line anticholinergic therapy. This study sought to compare the cost of onabotulinumtoxinA with other common pharmaceutical and medical device treatments for OAB.

- Based on a cost analysis undertaken from a US payer perspective, the annual cost of pharmacological medications for OAB treatment ranged from $500 to $3472. The annual cost of onabotulinumtoxinA is $1892, which was lower than that of all branded pharmaceutical treatments.
- OnabotulinumtoxinA was the least costly medical treatment for OAB therapy over 1, 5, and 10 years compared with sacral nerve stimulation and percutaneous tibial nerve stimulation.

[SNS]) or peripheral tibial nerve stimulation [PTNS]).[6] As healthcare costs rise in the United States, combined with the anticipated increase in the prevalence of OAB with the aging population, the cost of new therapies is a key driver of payers' reimbursement and access decisions. The main objective of this study is to compare, from a payer perspective, the cost of onabotulinumtoxinA injection with the costs of other OAB treatment in patients who are inadequately managed on an anticholinergic.

METHODS

An Excel-based cost model was developed to compare the annual costs of onabotulinumtoxinA 100 units (U) injection with 12 commonly used pharmaceutical treatments and 2 medical devices for OAB. Pharmaceutical treatments included Enablex (darifenacin) 7.5 mg daily; Toviaz (fesoterodine fumarate) 4 mg or 8 mg once daily; Myrbetriq (mirabegron) 50 mg once daily; oxybutynin chloride IR (immediate release) 5 mg twice daily; Ditropan XL (oxybutynin chloride extended release) 10 mg once daily; Gelnique (oxybutynin chloride) 10% gel once daily; Vesicare (solifenacin) 5 mg or 10 mg daily; tolterodine IR (immediate release) 2 mg twice daily; tolterodine LA (long acting) 4 mg once daily; Detrol LA (tolterodine long-acting) 4 mg once daily; trospium chloride IR 20 mg twice daily; and Sanctura XR (trospium chloride extended release) 60 mg once daily. Additional treatments for OAB included 2 medical devices, SNS device implantation and PTNS. These treatments were selected to reflect all of the FDA approved treatments (branded and generic) available to patients with OAB.

The analysis took the perspective of a commercial US payer and estimated the direct healthcare costs of each intervention. Direct healthcare costs included costs of the drug, procedural costs (where applicable), follow-up care, and AE costs (**TABLE 1**). Although each intervention is associated with a specific set of AEs, for the base case, only AE costs attributable to onabotulinumtoxinA were included. Drug acquisition cost for generic pharmaceutical medications were estimated using maximum allowable cost, a payer-specific negotiated rate. The maximum allowable cost rates were obtained from a survey of multiple insurers to provide an estimated national average (unpublished data). Cost for branded pharmaceutical medications was estimated to be 85% of the 2015 average wholesale price. The total cost of using pharmaceutical medications included drug costs and 2 annual physician visits for follow-up. Additionally, for mirabegron, it was assumed that 13% of patients would be prescribed metoprolol based on an analysis of MarketScan claims data, and these patients would require 1 additional physician visit to assess interactions with metoprolol (unpublished data on file). Medicare reimbursement rates were used to estimate costs associated with procedures, follow-up office visits, and office visits for management of AEs. Commercial costs were based on the estimation that private payer rates would be 122% of Medicare rates, based on a Medicare Payment Advisory Commission report in which Medicare rates averaged 82% of private payer rates in 2011.[10] Costs were evaluated over a 1-, 5-, and 10-year time horizon. For onabotulinumtoxinA compared with SNS and PTNS, the 5- and 10-year time horizon was of particular interest to ensure appropriate characterization of the introductory and maintenance phase costs of SNS and PTNS.

The cost of onabotulinumtoxinA included drug cost (100U) administered 1.72 times per year, based on the mean number of annual injections administered in a long-term extension study[11]; administration costs at the physician's office ($310.58 per injection procedure, based on 2015 Current Procedural Terminology [CPT] code 52287); 1 bladder scan (CPT 51798; $18.99); 1 follow-up physician visit (CPT 99213; $73.08) after each treatment cycle; and costs associated with UTI (12% per cycle) and urinary retention (6% per cycle), based on the reported AE rates compared with placebo in a phase 3 clinical trial.[12] The costs of a UTI were assumed to include the cost of 1 physician visit ($73.08) and 1 cycle of ciprofloxacin (500 mg, 10 tablets) at $3.00 per cycle.[13,14] The cost of urinary retention included 1 physician visit and 63 days of intermittent catheterization,[11] assuming the use of 4 catheters per day, at $1.85 per catheter.[15] All administration is assumed to occur in a physician outpatient office setting for the base-case analysis; however, previous research has indicated that in Europe, the cost of onabotulinumtoxinA may be largely attributable to treatment setting.[16] Thus,

Table 1. Overview of Annual Resource Utilization and Efficacy Parameters Related to Overactive Bladder Syndrome Therapies (2015 US Dollars)

Treatment	Drug Cost	Procedure Costs[a]	Physician follow-up visit costs[a]	AE costs	Total Annual Cost
Sacral nerve stimulation		See table below			$19,443 for year 1, $468 for years 2–10 revisions and programming $10,145 for battery replacement
Percutaneous tibial nerve stimulation	N/A	$3395 for year 1, $2114 for years 2–10	N/A	N/A	$3395 for year 1, $2114 for years 2–10
MYRBETRIQ (mirabegron)	$3076.28[b]	N/A	$189.90[c]	N/A	$3266.19
DETROL LA (solifenacin)	$3293.39[b]	N/A	$178.32	N/A	$3471.70
GELNIQUE (oxybutynin chloride)	$2777.18[b]	N/A	$178.32	N/A	$3254.60
ENABLEX (darifenacin)	$3018.21[b]	N/A	$178.32	N/A	$3196.52
VESIcare (solifenacin)	$2746.57	N/A	$178.32	N/A	$2924.89
TOVIAZ (fesoterodine fumarate)	$2603.54[b]	N/A	$178.32	N/A	$2781.85
SANCTURA XR (trospium chloride)	$2323.90[b]	N/A	$178.32	N/A	$2502.22
DITROPAN XL	$2156.40[b]	N/A	$178.32	N/A	$2334.71
OnabotulinumtoxinA	$956.32[d]	$651.72	$193.20	$90.38	$1891.62
Tolterodine LA	$1797.03[b]	N/A	$178.32	N/A	$1975.35
Tolterodine IR	$1534.05[b]	N/A	$178.32	N/A	$1712.37
Trospium chloride	$741.46[b]	N/A	$178.32	N/A	$919.77
Oxybutynin chloride IR	$321.42[b]	N/A	$178.32	N/A	$499.74

[a] Non-drug-related services inflated 22% based on MedPAC Report of Commercial to Medicare Payment Rates.[10]
[b] AWP minus 15%, assuming daily dosing.
[c] Assuming that 13% of mirabegron users would be prescribed metoprolol and require 1 additional physician visit to assess interactions, which increased the annual cost of mirabegron therapy by $11.59.
[d] Assuming 1.72 injections per year.
AE indicates adverse event; AWP, average wholesale price; IR, immediate release; LA, long-acting; N/A, not applicable; XL, extended release; XR, extended release.

administration in an ambulatory surgical center (ASC) ($801 per injection procedure) or hospital outpatient setting ($1297 per injection procedure) was explored in a sensitivity analysis. In this analysis, it was assumed that 60% of procedures took place in a physician's office, 25% in an ASC setting ($838.82), and 15% in a hospital outpatient setting ($1377.47). The cost of SNS included cost of the device, device eligibility testing by peripheral nerve evaluation (PNE) and/or staged implantation, cost of permanent implantation, device maintenance (assuming patients receive 2 reprogramming visits per year),[17] and cost of battery replacement at Year 7 (**TABLE 2**).[18,19]

For the base case, it was assumed that SNS device implantation was conducted at an ASC with a bundled payment for procedure and device. Only a proportion of patients (51%) evaluated for SNS ultimately received a permanent implant. This proportion was calculated as the sum of patients with successful PNE who move directly to surgical lead and battery placement, patients who fail PNE but respond to a staged trial and proceed to implantation, and patients who directly enter a 2-stage procedure (**FIGURE 1**).[20] Device replacement was assumed to occur at a rate of 3% per year.[18]

The cost of PTNS includes the cost of physician-office–based neurostimulation at a rate of $120.72 per visit (CPT 64566). Patients are assumed to receive weekly treatments for the first 12 weeks, with maintenance visits every 3.64 weeks thereafter, based on a median of 1.1 treatments per month reported among patients enrolled in the Sustained Therapeutic Effects of Percutaneous Tibial Nerve Stimulation study.[21] All patients were assumed to have complete adherence to prescribed therapy. For the base-case analysis, patient cost-sharing was not considered.

RESULTS

In the analysis of onabotulinumtoxinA compared with pharmaceutical therapies, total cost of anticholinergics over 1 year ranged from $500 (oxybutynin chloride IR to $3472 (Detrol LA), and the cost of mirabegron was $3266. At years 5 and 10, respectively, the costs of anticholinergic treatment ranged from $2500 and $5000 (oxybutynin chloride IR), to $17,360 and $34,720 (Detrol LA), and the costs of mirabegron were $16,330 and $32,660. OnabotulinumtoxinA was associated with a total annual cost of $1892—a lower annual cost than all branded medications included in the analysis, but more costly than 3 of the 4 generic anticholinergics (tolterodine tartrate IR, trospium chloride IR, and oxybutynin chloride IR) included in the analysis. In the sensitivity analysis exploring the impact of onabotulinumtoxinA administration split between the physician office (60%),

Table 2. Probability of Sacral Nerve Stimulation Device Implantation and Weighted Average Costs of Test and Device Implantation (Medicare 2014 Reimbursement Rates)

	Cost ($, per patient)	Probability	Weighted average cost ($, per patient)
Year 1 cost (test + permanent implantation costs)			
Sacral nerve stimulation device probabilities			
Distribution of test techniques	N/A	(21.0% PNE only) + (3.9% PNE and staged) + (75.1% staged only)	N/A
Probability of permanent implantation[19]	N/A	(48% PNE only) + (64.8% PNE and staged) + (51% staged only)	N/A
Testing cost inputs			
PNE only (CPT 64561physician + facility)	$4099.44[25]	21.04%[19]	$862.52[25]
Stage 1 (CPT 64581physician + facility)	$6980.20[25]	75.1%[19]	$5242.13[25]
PNE (CPT 64561physician + facility) and stage 1 (CPT 64581physician + facility)	$11,079.64	3.86%[19]	$427.68[25]
Total test cost	N/A	N/A	$6532.33
Permanent implantation cost inputs (probability 50.9%)			
Permanent implantation after PNE only (CPTs 64581, 64590)	$23,315.90[17]	48%[19]	$2356.04[25]
Permanent implantation after stage 1 (CPT 64590)	$16,335.70[17]	50.9%[19]	$6256.72[25]
Permanent implantation after PNE and stage 1 (CPT 64590)	$16,335.70[17]	64.8%[19]	$408.30[25]
Analysis/programming, 2x[16] (CPT 95972)	$219.96[17]	50.9%[19]	$111.97[25]
Revision of electrode array (CPT 64585)	$1091.93[17]	4%[17]	$22.21[25]
Revision of generator (CPT 64595)	$16,335.70[17]	3%[17]	$249.50[25]
Total permanent implantation cost	N/A	N/A	$9,404.74
Total year 1 cost (Medicare)[25]	N/A	N/A	$15,937.07
Years 2–6 cost (maintenance)			
Maintenance costs (probability 50.9%)			
Analysis/programming, 2x16 (CPT 95972)	$219.96[25]	50.9%	$111.97[25]
Revision of electrode array (CPT 64585)	$1091.93[25]	4%[17]	$22.21[25]
Revision of generator (CPT 64595)	$16,335.70[25]	3%[17]	$249.50[25]
Total annual maintenance costs (Years 2–6) (Medicare)[25]	N/A	N/A	$383.68
Year 7 cost (maintenance + battery replacement costs)			
Battery replacement, Year 7[a] (CPT 64590)	$16,335.70[25]	50.9%	$8315.73[25]
Total Year 7 cost (Medicare)[25]	N/A	N/A	$8315.73

CPT indicates current procedural terminology; N/A, not applicable; PNE, percutaneous nerve evaluation.
[a]Assumed to occur at Year 7; however, newer battery models may require replacement at 5 years.[18]

ASC (25%), and hospital outpatient (15%) settings, the total annual cost for onabotulinumtoxinA treatment was $2505, which was still less expensive than all branded medications except for Sanctura XR and Ditropan XL, and more costly than the 4 generic anticholinergics (**FIGURE 2**).

In the analysis that compared onabotulinumtoxinA 100U injection procedure with device treatments, year 1 costs were $1892 (onabotulinumtoxinA), $3395 (PTNS), and $19,443 (SNS). At years 5 and 10, respectively, the costs were as follows: $9458 and $18,916 (onabotulinumtoxinA); $11,849 and $21,316 (PTNS); and $21,316 and $33,801 (SNS) (**FIGURE 3**). The first-year cost of SNS was approximately 10 times higher than that of onabotulinumtoxinA due to the high initial cost of testing and device implantation. While costs for SNS were reduced in subsequent years, the total 5- and 10-year costs for SNS remained the highest of all the treatments evaluated.

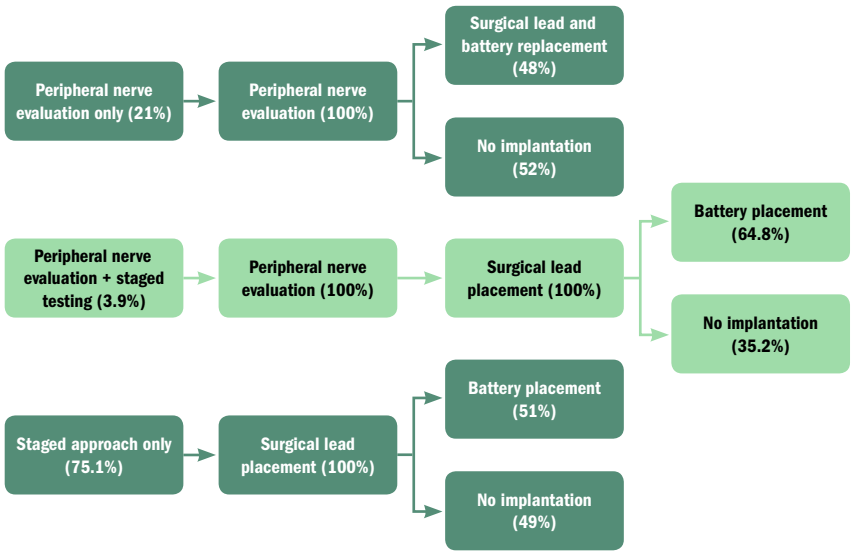
DISCUSSION

Results from this study suggest that the total annual cost of onabotulinumtoxinA treatment for OAB patients who are inadequately managed on an anticholinergic is lower than the annual costs of the most commonly used branded pharmaceutical agents, and of the costs

of SNS and PTNS, both in the short and long term. As expected, costs for onabotulinumtoxinA were higher than the costs of generic anticholinergics included in the analysis.

The cost of pharmaceutical medications included drug costs and 2 annual physician visits for follow-up. Additionally, for mirabegron, it was assumed that 13% of patients would be prescribed metoprolol, and would require 1 additional physician visit to assess interactions. The marginal increased cost of $11.59 associated with the extra office visit was negligible, and accounts for less than 0.4% of the total annual cost of mirabegron therapy ($3266.19). The model did not include costs due to AEs for pharmaceutical treatments. The inclusion of AEs for onabotulinumtoxinA, but not for pharmaceutical comparators, resulted in an overestimate for cost of onabotulinumtoxinA in comparison with the costs of pharmaceutical treatments. The assumption of battery replacement at 7 years for SNS may be conservative, as newer smaller batteries, based on usage, last 2.9 to 5.4 years.[19] More frequent battery replacement of every 5 years for SNS yields an even less favorable long-term cost ($43,946 for SNS over 10 years).

Figure 1. Patient Flow Diagram for Overactive Bladder Syndrome Patients Undergoing Peripheral Nerve Evaluation



Furthermore, the SNS costing paradigm assumed that 49% of patients evaluated for SNS fail the testing phase and do not receive permanent battery implantation[20]; therefore, only 51% of patients incur the full cost of SNS therapy. The costs of SNS would increase significantly if the model assumed that 100% of patients ultimately receive permanent battery implantation.

One limitation to this analysis was the assumption of 100% adherence and persistence to treatments. The assumption of perfect adherence and persistence may overestimate the cost of treatments due to nonadherence or treatment discontinuation. In addition, no patient cost-sharing,

Figure 2. Annual Commercial Cost to Payer of Pharmaceutical Treatment Options for Overactive Bladder Syndrome Compared With Cost of OnabotulinumtoxinA

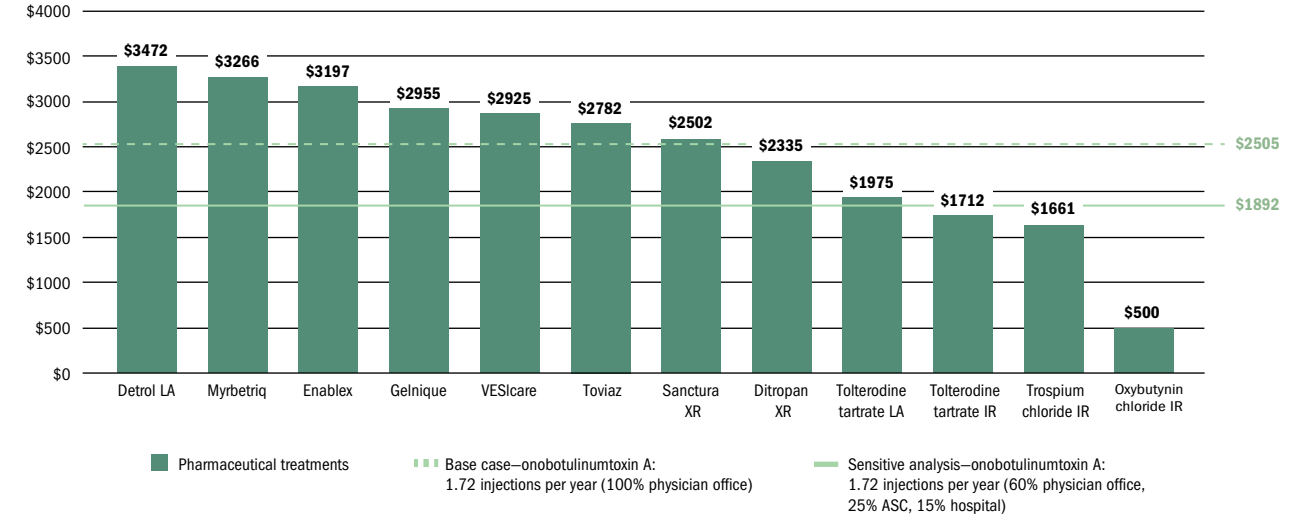
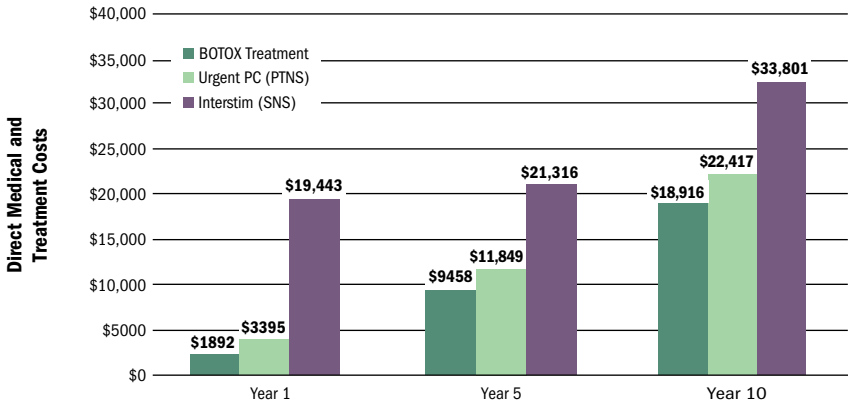


Figure 3. Annual Commercial Cost to Payer of Medical Devices for Overactive Bladder Syndrome Compared With Cost of OnabotulinumtoxinA



PC indicates prodecure cost; PTNS, percutaneous tibial nerve stimulation; SNS, sacral nerve stimulation.

product rebating, or discounts were included in the base case, which may overestimate the actual treatment costs to health plans. A discount factor was not applied to the 5- and 10-year time horizons. Moreover, this analysis only evaluated the direct treatment costs; therefore, potential cost savings due to healthcare resource offset associated with treatments were not considered in this analysis or included in the model. A future in-depth evaluation comparing the various approaches and assumptions across the relevant research conducted to date could provide a greater understanding of cost drivers in OAB.

Our findings that onabotulinumtoxinA may be cost-saving compared with branded OAB medications therapy are corroborated by a National Institutes of Health–funded cost-effectiveness model of onabotulinumtoxinA versus solifenacin- and trospium-branded anticholinergics.[22] The economic endpoints used to populate the model were obtained from a randomized, double-blind, active-comparator study of the impact of onabotulinumtoxinA on UI (also referred to as the ABC study).[23] In this cost-effectiveness model, the 6-month cost of onabotulinumtoxinA was $1270 compared with $1340 for anticholinergics, with better rates of UI resolution for onabotulinumtoxinA observed (eg, 27% of patients taking onabotulinumtoxinA achieved continence compared with 13% of patients on anticholinergics). The results of our analysis also support the findings of prior pharmacoeconomic studies evaluating the use of onabotulinumtoxinA for OAB patients. An analysis by Watanabe et al reported an average year 1 onabotulinumtoxinA cost of $2626 compared with $23,614 for SNS and $11,637 for augmentation cystoplasty (2007 US$).[24] OnabotulinumtoxinA remained the least costly treatment option in the analysis of 2- and 3-year cumulative costs, and it was less costly than SNS in the all-scenario analyses. Siddiqui and colleagues evaluated the cost-effectiveness of onabotulinumtoxinA compared with SNS in OAB patients from a US societal perspective. The authors reported lower 2-year cumulative costs for onabotulinumtoxinA ($4392) compared with SNS ($15,743), and concluded that over a 2-year period, onabotulinumtoxinA was cost-effective compared with SNS for the treatment of refractory urgency UI.[25] While the methods across all of these studies vary considerably, their overall conclusions are consistent with our findings.

CONCLUSIONS

This analysis suggests that short- and long-term costs of the current treatment options vary considerably in OAB patients who are inadequately managed on an anticholinergic. OnabotulinumtoxinA was the least costly option among the injection procedure and medical device treatments; when it was administered in the outpatient setting, it was less costly than all branded pharmaceutical treatments. Although cost is an important component when comparing these treatments, other aspects such as efficacy and safety must be considered when deciding on an appropriate treatment of OAB. ajpb

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REFERENCES

1. Haylen BT, de Ridder D, Freeman RM, et al; International Urogynecological Association; International Continence Society. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. *Neurourol Urodyn.* 2010;29(1):4-20. doi: 10.1002/nau.20798.
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):327-336.
3. Cheung WW, Khan NH, Choi KK, Bluth MH, Vincent MT. Prevalence, evaluation and management of overactive bladder in primary care. *BMC Fam Pract.* 2009;10:8. doi: 10.1186/1471-2296-10-8.
4. Coyne KS, Margolis MK, Kopp ZS, Kaplan SA. Racial differences in the prevalence of overactive bladder in the United States from the epidemiology of LUTS (EpiLUTS) study. *Urology.* 2012;79(1):95-101. doi: 10.1016/j.urology.2011.09.010.
5. Ganz ML, Smalarz AM, Krupski TL, et al. Economic costs of overactive bladder in the United States. *Urology.* 2010;75(3):526-532,532.e1-e18. doi: 10.1016/j.urology.2009.06.096.

6. Gormley EA, Lightner DJ, Faraday M, Vasavada SP; American Urological Association; Society of Urodynamics, Female Pelvic Medicine. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline amendment. *J Urol.* 2015;193(5):1572-1580. doi: 10.1016/j.juro.2015.01.087.
7. Chancellor MB, Migliaccio-Walle K, Bramley TJ, Chaudhari SL, Corbell C, Globe D. Long-term patterns of use and treatment failure with anticholinergic agents for overactive bladder. *Clin Ther.* 2013;35(11):1744-1751. doi: 10.1016/j.clinthera.2013.08.017.
8. Benner JS, Nichol MB, Rovner ES, et al. Patient-reported reasons for discontinuing overactive bladder medication. *BJU Int.* 2010;105(9):1276-1282. doi: 10.1111/j.1464-410X.2009.09036.x.
9. Jundt K, Schreyer K, Friese K, Peschers U. Anticholinergic therapy: do the patients take the pills prescribed? *Arch Gynecol Obstet.* 2011;284(3):663-666. doi: 10.1007/s00404-010-1720-x.
10. Medicare Payment Advisory Commission. Report to the Congress: Medicare payment policy. 2011. http://www.medpac.gov/docs/default-source/reports/Mar11_EntireReport.pdf?sfvrsn=0. Accessed December 4, 2017.
11. Chartier-Kastler E, Nitti V, De Ridder D, et al, Durable improvements in urinary incontinence and positive treatment response in patients with idiopathic overactive bladder syndrome following long-term onabotulinumtoxinA treatment: Final results of 3.5-year study, *Prog Urol*. 2015 Nov; 25 (13): 739. doi: 10.1016/j.purol.2015.08.047.
12. Botox [prescribing information]. Irvine, CA: Allergan, Inc; 2015.
13. Cipro [prescribing information]. Wayne, NJ: Bayer HealthCare Pharmaceuticals Inc; 2011.
14. Red Book Online®. MICROMEDEX® 2.0, Truven Health Analytics Inc. http://www.micromedexsolutions.com.ucsf.idm.oclc.org/micromedex2/librarian/CS/9446C9/ND_PR/evidencexpert/ND_P/evidencexpert/DUPLICATION-SHIELDSYNC/CE12BC/ND_PG/evidencexpert/ND_B/evidencexpert/ND_AppProduct/evidencexpert/ND_T/evidencexpert/PFActionId/redbook.FindRedBook?navitem=topRedBook&isToolPage=true. Accessed May 18, 2015.
15. Medicare pricing, data analysis, and coding. Noridian Healthcare Solutions, LLC, website. dmepdac.com/dmecsapp/do/feesearch. Accessed June 24, 2013.
16. Ruff L, Bagshaw E, Aracil J, Velard ME, Pardhanani G, Hepp Z. Economic impact of onabotulinumtoxinA for overactive bladder with urinary incontinence in Europe. *J Med Econ.* 2016;19(12):1107-1115.
17. Burks FN, Diokno AC, Lajiness MJ, Ibrahim IA, Peters KM. Sacral neuromodulation reprogramming: is it an office burden? *Int Urogynecol J Pelvic Floor Dysfunct.* 2008;19(8):1137-1140. doi: 10.1007/s00192-008-0601-3.
18. Arlandis S, Castro D, Errando C, et al. Cost-effectiveness of sacral neuromodulation compared to botulinum neurotoxin A or continued medical management in refractory overactive bladder. *Value Health.* 2011;14(2):219-228. doi: 10.1016/j.jval.2010.08.006.
19. InterStim and InterStim II neurostimulator features and specifications. Medtronic website. professional.medtronic.com/pt/uro/snm/prod/interstim/index.htm#.VvQSwulrKUk. Accessed May 18, 2015.
20. Cameron AP, Anger JT, Madison R, Saigal CS, Clemens JQ; Urologic Diseases in America Project. National trends in the usage and success of sacral nerve test stimulation. *J Urol.* 2011;185(3):970-975. doi: 10.1016/j.juro.2010.10.060.
21. Peters KM, Carrico DJ, Wooldridge LS, Miller CJ, MacDiarmid SA. Percutaneous tibial nerve stimulation for the long-term treatment of overactive bladder: 3-year results of the STEP study. *J Urol.* 2013;189(6):2194-2201. doi: 10.1016/j.juro.2012.11.175.
22. Zyczynski H. Comparison of cost-effectiveness of onabotulinumtoxin A and anticholinergic medications for the treatment of urgency urinary incontinence [paper presentation abstract 02]. *Female Pelvic Med Reconstr Surg.* 2013;19(Suppl 2):S45. doi: 10.1097/SPV.0b013e3182a5ddf0
23. Visco AG, Brubaker L, Richter HE, et al; Pelvic Floor Disorders Network. Anticholinergic therapy vs. onabotulinumtoxina for urgency urinary incontinence. *N Engl J Med.* 2012;367(19):1803-1813. doi: 10.1056/NEJMoa1208872.
24. Watanabe JH, Campbell JD, Ravelo A, Chancellor MB, Kowalski J, Sullivan SD. Cost analysis of interventions for antimuscarinic refractory patients with overactive bladder. *Urology.* 2010;76(4):835-840. doi: 10.1016/j.urology.2010.01.080.
25. Siddiqui NY, Amundsen CL, Visco AG, Myers ER, Wu JM. Cost-effectiveness of sacral neuromodulation versus intravesical botulinum A toxin for treatment of refractory urge incontinence. *J Urol.* 2009;182(6):2799-2804. doi: 10.1016/j.juro.2009.08.031.

eAPPENDIX

eAppendix Table 1. Total Cost of Sacral Nerve Stimulation to a Medicare and a Commercial Payer

Perspective	Cost (US$, per patient)		
	Test + permanent implantation costs (year 1)	Per-year device maintenance costs (years 2-6)	Year 7 cost (maintenance + battery replacement costs)
Medicare[25]	$15,937.07	$383.68	$8315.73
Commercial (122% of Medicare)[a]	$19,443.23	$468.09	$10,145.19

[a]Commercial costs were based on the estimation that private payer rates would be 122% of Medicare rates, based on a Medicare Payment Advisory Commission report in which Medicare rates averaged 82% of private payer rates in 2011.[10]

eAppendix Table 2. OnabotulinumtoxinA Costs per Injection Cycle to a Medicare Payer

	Cost (US$, per patient)	Probability	Weighted average cost (US$, per patient)
Bladder injection (CPT 52287)	$310.58[26]	100%	$310.58[26]
OnabotulinumtoxinA injection (100 U per injection)	$556.00[14]	100%	$556.00[14]
Physician follow-up visits (CPT 99213)	$73.08[26]	100%	$73.08[26]
Bladder ultrasound (CPT 51798)	$18.99[26]	100%	$18.99[26]
Urinary tract infection prescription[a]	$76.08[14,26]	12%[12]	$9.13[14,26]
Urinary retention[b]	539.28[15]	6%[12]	$32.36[15]
Cost per cycle	N/A	N/A	$1000.14
Total yearly cost (1.72 injection cycles)	N/A	N/A	$1720.24

[a]Urinary tract infection prescription includes 1 physician visit + 1 cycle of ciprofloxacin (500 mg, 10 tablets) at $3.60/cycle.

[b]Urinary retention costs include 63 days of clean intermittent catheterization x 4 catheters/day × $1.83 per catheter (Healthcare Common Procedure Coding System A351).

CPT indicates Current Procedural Terminology; N/A, not applicable; U, units.

eAppendix Table 3. Sacral Nerve Stimulation Device Implantation: Medicare Costs

Cost Input	CPT Code and Description	Cost[a]
Peripheral nerve evaluation	CPT 64561: Percutaneous implantation of neurostimulator electrode array; sacral nerve including guidance if performed[25] Ambulatory surgical center facility + physician fee[27]	$3691.78
Stage 1 evaluation (advanced)	CPT 64581: Incision for implantation of neurostimulator electrode array; sacral nerve (transforaminal placement)[25] Ambulatory surgical center facility + physician fee[27] (Note: fluoroscopy, CPT 76000-26, cost not included)	$6980.20
Permanent implantation (note: Stage 1 patients will only have CPT 64590)	CPT 64581: see description above[25] CPT 64590: Insertion or replacement of peripheral or gastric neurostimulator pulse generator or receiver, direct or inductive coupling[25] Ambulatory surgical center facility + physician fee[27]	CPT 64581: $6980.20 CPT 64590: $16,335.70 Total: $23,315.90
Follow-up analysis/programming visits (100%,[b] 2 times per year, 1 hour each)[16]	CPT 95972: Electronic analysis of implanted neurostimulator pulse generator system; complex spinal cord or peripheral neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming, first hour[25]	$109.98
Battery replacement (100%[b] in year 7)[17]	CPT 64590: Revision or removal of peripheral or gastric neurostimulator pulse generator or receiver[25]	$16,335.70
Revision/removal of the electrode array (4% every year)[17]	CPT 64585: Revision or removal of peripheral neurostimulator electrode array[25]	$1091.93
Revision/removal of neurostimulator pulse	CPT 64595: Revision or removal of peripheral or gastric neurostimulator pulse generator or receiver[25]	$16,335.70

generator or receiver (3% every year)[17]		

CPT indicates current procedural terminology.

[a]Unweighted per-patient costs of physician, procedure, and facility.

[b]One hundred percent of the patients who underwent an implantation of the InterStim® sacral nerve stimulation device.

eAppendix Table 4. Probability of Sacral Nerve Stimulation Device Implantation and Weighted Average Costs of Test and Device Implantation (Medicare 2014 reimbursement rates)

	Cost (US$, per patient)	Probability	Weighted average cost (US$, per patient)
Year 1 cost (test + permanent implantation costs)			
Sacral nerve stimulation device probabilities			
Distribution of test techniques	N/A	(21.0% PNE only) + (3.9% PNE and staged) + (75.1% staged only)	N/A
Probability of permanent implantation[19]	N/A	(48% PNE only) + (64.8% PNE and staged) + (51% staged only)	N/A
Testing cost inputs			
PNE only (CPT 64561 physician + facility)	$4099.44[25]	21.04%[19]	$862.52[25]
Stage 1 (CPT 64581 physician + facility)	$6980.20[25]	75.1%[19]	$5242.13[25]
PNE (CPT 64561 physician + facility) and stage 1 (CPT 64581 physician + facility)	$11,079.64	3.86%[19]	$427.68[25]
Total test cost	N/A	N/A	$6532.33
Permanent implantation cost inputs (probability 50.9%)			

	Cost (US$, per patient)	Probability	Weighted average cost (US$, per patient)
Permanent implantation after PNE only (CPTs 64581, 64590)	$23,315.90[17]	48%[19]	$2356.04[25]
Permanent implantation after stage 1 (CPT 64590)	$16,335.70[17]	50.9%[19]	$6256.72[25]
Permanent implantation after PNE and stage 1 (CPT 64590)	$16,335.70[17]	64.8%[19]	$408.30[25]
Analysis/programming, 2x[16] (CPT 95972)	$219.96[17]	50.9%[19]	$111.97[25]
Revision of electrode array (CPT 64585)	$1091.93[17]	4%[17]	$22.21[25]
Revision of generator (CPT 64595)	$16,335.70[17]	3%[17]	$249.50[25]
Total permanent implantation cost	N/A	N/A	$9404.74
Total year 1 cost (Medicare)[25]	**N/A**	**N/A**	**$15,937.07**
Years 2-6 cost (maintenance)			
Maintenance costs (probability 50.9%)			
Analysis/programming, 2x[16] (CPT 95972)	$219.96[25]	50.9%	$111.97[25]
Revision of electrode array (CPT 64585)	$1091.93[25]	4%[17]	$22.21[25]
Revision of generator (CPT 64595)	$16,335.70[25]	3%[17]	$249.50[25]
Total annual maintenance costs (Years 2-6) (Medicare)[25]	**N/A**	**N/A**	**$383.68**

	Cost (US$, per patient)	Probability	Weighted average cost (US$, per patient)
Year 7 cost (maintenance + battery replacement costs)			
Battery replacement, Year 7[a] (CPT 64590)	$16,335.70[25]	50.9%	$8315.73[25]
Total Year 7 cost (Medicare)[25]	N/A	N/A	**$8315.73**

CPT indicates current procedural terminology; N/A, not applicable; PNE, percutaneous nerve evaluation.

[a]Assumed to occur at Year 7; however, newer battery models may require replacement at 5 years.[18]