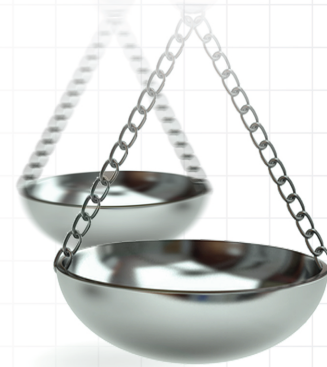




Cost-effectiveness of overactive bladder treatments from a US commercial and payer perspective

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Aim: The cost-effectiveness of treatment options (anticholinergics, β 3-adrenoceptor agonists, onabotulinumtoxinA, sacral nerve stimulation and percutaneous tibial stimulation [the latter two including new rechargeable neurostimulators]) for the management of overactive bladder (OAB) were compared with best supportive care (BSC) using a previously published Markov model. **Materials & methods:** Cost-effectiveness was evaluated over a 15-year time horizon, and sensitivity analyses were performed using 2- and 5-year horizons. Discontinuation rates, resource utilization, and costs were derived from published sources. **Results:** Using Medicare and commercial costs over a 15-year time period, onabotulinumtoxinA 100U had incremental cost-effectiveness ratios (ICERs) gained of \$39,591/quality-adjusted life-year (QALY) and \$42,255/QALY, respectively, versus BSC, which were the lowest ICERs of all assessed treatments. The sensitivity analyses at 2- and 5-year horizons also showed onabotulinumtoxinA to be the most cost-effective of all assessed treatments versus BSC. **Conclusion:** OnabotulinumtoxinA 100U is currently the most cost-effective treatment for OAB.

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Overactive bladder (OAB) is a chronic disorder characterized by urinary urgency, increased urinary frequency and nocturia, which may be accompanied by urgency urinary incontinence [1,2]. The overall prevalence of OAB is similar between men (16.0%) and women (16.9%), and it increases with age [3]. Given the prevalence and chronic nature of OAB, the costs associated with OAB are considerable, with an estimated cost of US \$82.6 billion in 2020 [4]. Patients with OAB may receive initial treatment with behavioral therapy including dietary modifications, pelvic floor exercises and supportive care (e.g., incontinence pads); however, treatment often progresses to pharmacotherapy [5–7]. OAB patients treated with oral anticholinergics often cycle through multiple therapies without adequate symptom relief [8], further exacerbating healthcare expenditures and reducing patient health-related quality of life [9]. With only 5–47% of patients with OAB persisting on anticholinergics at 1 year, patients who are inadequately treated with anticholinergics represent a considerable challenge in the management of OAB [10]. Alternative treatment options for these patients include β 3-adrenoceptor agonists, intradetrusor onabotulinumtoxinA, implantable sacral nerve stimulation (SNS) and percutaneous tibial nerve stimulation (PTNS) [5,6].

In order to compare the value of OAB treatments within the USA, a Markov model was developed in 2016 to estimate the cost-effectiveness of anticholinergics (solifenacin and tolterodine), mirabegron, onabotulinumtoxinA 100U (BOTOX[®], Allergan, an AbbVie company, CA, USA), SNS (InterStim[™]; Medtronic plc, MN, USA) and

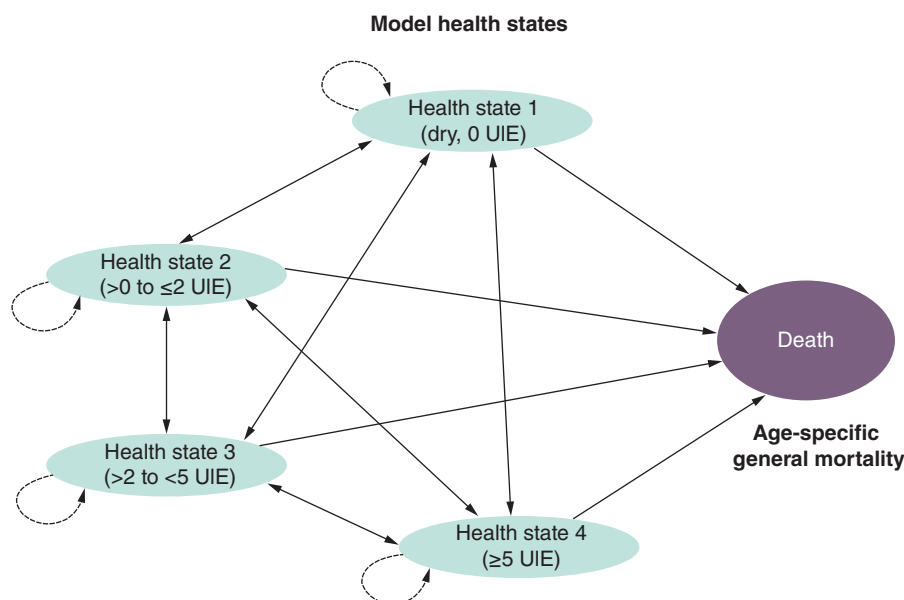


Figure 1. Model diagram and health states. At baseline and at the end of model cycle 1 (week 12), patients are distributed across health states 1–4 as observed from the pooled onabotulinumtoxinA 100U trial patient level. Patients receive either best supportive care (BSC) or whichever comparator is selected. Patients assigned to BSC remain on this treatment for the duration of the model. Patients assigned to the selected comparator remain on that treatment if they respond; if they do not respond, they revert to BSC for the duration of the model. Figure is reprinted with permission from Murray *et al.* (2019) [11]. UIE: Urinary incontinence episode.

PTNS (Urgent[®] PC; Laborie Medical Technologies, MA, USA), versus best supportive care (BSC) [11]. Treatment with onabotulinumtoxinA produced the largest gain in quality-adjusted life-years (QALYs; 7.179) and the lowest estimated incremental cost–effectiveness ratio (ICER; \$32,680/QALY) of all assessed treatments compared with BSC. Thus, onabotulinumtoxinA was found to be the most cost-effective treatment option for patients with OAB. Since the publication of this original cost–effectiveness model, there have been recent additions to the OAB therapeutic landscape. These include a new β 3-adrenoceptor agonist, vibegron 75 mg (Gemtesa[®]; Urovant Sciences, Inc., CA, USA) [12], that received US FDA approval in December 2020. Furthermore, new rechargeable neurostimulators recently emerged, including an SNS device from Axonics (r-SNM[®]; Axonics Modulation Technologies, CA, USA) [13] and InterStim[™] Micro (Medtronic plc, MN, USA). The InterStim Micro neurostimulator is 50% smaller than Axonics r-SNM system, and it shares the same proposed life expectancy of 15 years [14]. InterStim[™] II, a nonrechargeable system with a life expectancy of 5–7 years [15], was also introduced since publication of the original model. Finally, Protect PNS[™] (Uro Medical Inc, FL, USA) is a new, wireless tibial neuromodulation device currently under investigation.

Given the potential implications of these new treatments in the management of OAB in clinical practice, we conducted an updated assessment of the cost–effectiveness of currently available treatment options (anticholinergics, mirabegron, vibegron, intradetrusor onabotulinumtoxinA, SNS [r-SNM, InterStim II, InterStim Micro] and PTNS [Urgent[®] PC, Protect PNS]) versus BSC.

Materials & methods

Model structure

The structure of the Markov model used in this cost–effectiveness analysis has been previously published [11] (Figure 1). The model is composed of five health states (i.e., 0 urinary incontinence episodes [UIEs]/day, >0 and ≤2 UIEs/day, >2 and <5 UIEs/day, ≥5 UIEs/day, and dead [acts as an absorbing state that cannot be exited]). The duration of the model cycle was set at 3 months, with the base case employing a 15-year time horizon with an annual discount rate of 3% from a Medicare payer perspective. The base-case analyses were evaluated over a 15-year time horizon to allow a valid comparison with InterStim Micro and Axonics r-SNM, with sensitivity analyses at 2 and 5 years. Cost–effectiveness was assessed from a Medicare perspective (as in the previous model)

Table 1. Overview of updated and original Markov model.

Base-case parameters	Original model	Updated model
Population	US adults with OAB who were not adequately managed with anticholinergics	US adults with OAB who were not adequately managed with anticholinergics
Comparators	Best supportive care Anticholinergic – Solifenacin 5 mg and 10 mg – Tolterodine ER 4 mg Mirabegron 25 mg and 50 mg OnabotulinumtoxinA 100U SNS InterStim (Medtronic) PTNS, urgent PC	Anticholinergic – Solifenacin 5 mg and 10 mg – Tolterodine ER 4 mg – Branded + generic Generic only Best supportive care Mirabegron: 25 mg and 50 mg Vibegron 75 mg OnabotulinumtoxinA 100U SNS, InterStim II (Medtronic) SNS, InterStim Micro (Medtronic) SNS (Axonics) PTNS, Urgent PC PTNS, Protect PNS
Time horizon	10-year horizon	15-year horizon, and sensitivity for 2- and 5-year horizons
Perspective	Medicare	Medicare or commercial [†]
Cost inputs	Medical and pharmacy costs (2016)	Medical and pharmacy costs (2020)
Outcomes	Total cost Quality-adjusted life-years Cost per urinary incontinence episodes avoided Incremental cost-effectiveness ratio	Total cost Quality-adjusted life-years Cost per urinary incontinence episodes avoided Incremental cost-effectiveness ratio

[†] Commercial costs are inflated based on Medicare Payment Advisory Commission report [16].
ER: Extended release; OAB: Overactive bladder; PTNS: Percutaneous tibial nerve stimulation; SNS: Sacral nerve stimulation.

and a commercial perspective (inflated costs based on the Medicare Payment Advisory Commission report [16]). The primary changes to the original Markov model are summarized in Table 1.

Model comparators & BSC

Based on a 3-month treatment cycle, the model evaluated anticholinergics (solifenacin 5 or 10 mg, tolterodine extended release [ER], generic anticholinergics, generic and branded anticholinergics), mirabegron 25 or 50 mg, vibegron 75 mg, onabotulinumtoxinA 100U, SNS devices (Medtronic InterStim II, InterStim Micro, Axonics r-SNM system), and PTNS (Urgent PC, Protect PNS), compared with a BSC reference therapy that entailed behavioral therapy and urinary incontinence pads. New assumptions to the model included the removal of anticholinergic use from the BSC arm to better reflect clinical practice based on expert opinion. Patients assigned to a treatment option remained on that treatment if they responded (i.e., $\geq 50\%$ reduction in UIEs), and nonresponders reverted to BSC for the duration of the model. For treatments included in the original model, the proportions of patients in cycle 1 remained the same as previously [11], and assumptions for the newer treatments are in Supplementary Table 1. For vibegron, the proportion of patients was assumed to be the same as for mirabegron across the different health states, and the proportion of patients for oral anticholinergics was assumed to be the same as that for solifenacin 10 mg. Transition probabilities remained the same as in the previous model [11].

Data sources, assumptions & inputs

QALYs were calculated from efficacy, discontinuation rate and utility sources. Efficacy data for the oral pharmacotherapies (anticholinergics and $\beta 3$ -adrenoceptor agonists) were derived from a published network meta-analysis [17]. Efficacy and utilities for generic only and branded and generic anticholinergic medications were assumed to be the same as for solifenacin (highest efficacy) while vibegron was assumed to be similar to mirabegron 50 mg based on current published clinical trial data. Discontinuation rates for oral pharmacotherapies were also derived from the same previously published network meta-analysis [18]. Efficacy and discontinuation data for onabotulinumtoxinA were based on the two pivotal phase III clinical trials [19,20] and a long-term extension study

of these trials [21]. Efficacy and safety inputs for SNS devices were based on published clinical trial data [14,22–25]. InterStim II and InterStim Micro were assumed to be identical and based on the latest published InterStim trial data [22,23,26]. Similarly, PTNS efficacy inputs were based on their trial data [27–30]. A 60-month duration for PTNS therapy was based on a National Institute for Health and Clinical Excellence recommendation that PTNS be used for medium-term duration due to lack of longer-term data [31,32]. Utility values were derived by mapping I-QOL scores to the EQ-5D using a pre-existing algorithm [33].

Resource and pharmacy costs were included as previously described [11] but were updated to reflect 2020 costs [16,34]. The updated costs for this model from a Medicare and commercial perspective are summarized in Table 2. Resource utilization and cost data were derived from the same published sources in the original model [27–29,33,35–38] plus recent sources to account for updated medical and pharmacy costs for 2020 [34,39,40], costs and battery life duration for the rechargeable SNS devices [13], and costs for Protect PNS [30]. Costs for the Medtronic InterStim II and InterStim Micro and Axonics r-SNM system were assumed to be the same, using the cost for the implant procedure [41]. In terms of cost assumptions, anticholinergic prices were calculated as the wholesale acquisition price minus 15%, and costs for ‘brand and generic’ and ‘generic only’ arms were based on weighted market share. Finally, in contrast to the original model, which included the cost of battery replacement at the end of the last year of device life expectancy, the new model included the cost of battery replacement at the beginning of the year following the end of device life expectancy.

Model outcomes

Outcomes reported included total and incremental QALYs and costs, and ICERs relative to BSC. The change in utility value induced by a treatment was multiplied by the duration of the treatment effect to provide the number of QALYs gained [42]. An ICER is used to compare the cost–effectiveness of two competing technologies (e.g., A and B), and it is calculated using the formula: $(\text{Cost A} - \text{Cost B}) / (\text{Effectiveness A} - \text{Effectiveness B})$. ICER is a measure of the cost per unit increase in effectiveness (e.g., QALY), and an ICER of \$100,000–\$150,000/QALY is considered cost-effective in the USA [43]. The base-case analysis used the upper and lower ICER limits as a measure of cost–effectiveness.

Results

Base-case analyses: 15-year time horizon

In the base-case scenario using Medicare costs over a 15-year time horizon, onabotulinumtoxinA 100U was the most cost-effective OAB treatment vs BSC with an ICER of \$39,591/QALY (Table 3 and Figure 2). The β 3-adrenoceptor agonists were the least cost-effective OAB treatments vs BSC, with ICERs of \$1.47 million/QALY (mirabegron 25 mg), \$1.29 million/QALY (mirabegron 50 mg) and \$1.61 million/QALY (vibegron 75 mg). The ICER for the ‘brand and generic’ anticholinergic arm vs BSC was \$324,658/QALY, which was approximately eight-times higher than that for onabotulinumtoxinA. Comparatively, the ICER for the ‘generic only’ anticholinergic arm was \$158,866/QALY, which was approximately four times higher than that for onabotulinumtoxinA. Neither of the rechargeable SNS devices were cost-effective vs BSC, with ICERs of \$229,891/QALY and \$163,783/QALY for the InterStim Micro and r-SNM system, respectively; however, Urgent PC (\$98,031/QALY) and Protect PNS (\$69,027/QALY) were cost-effective vs BSC.

In the base-case scenario using commercial costs at a 15-year time horizon, onabotulinumtoxinA 100U was again the most cost-effective OAB treatment vs BSC, with an ICER of \$42,255/QALY (Table 4 and Figure 3). The β 3-adrenoceptor agonists were the least cost-effective OAB treatment vs BSC with ICERs >\$1,000,000/QALY. The ICER for the ‘brand and generic’ and ‘generic only’ anticholinergic arms were similar to that reported from a Medicare payer perspective (\$321,862/QALY and \$156,070/QALY), while the ICER for rechargeable SNS devices were approximately \$40,000 to \$50,000/QALY higher than the Medicare costs. Protect PNS (\$69,200/QALY) was cost-effective vs BSC based on the willingness-to-pay threshold of \$100,000/QALY, while Urgent PC (\$122,446/QALY) was cost-effective when the higher threshold of \$150,000/QALY was considered.

In both Medicare and commercial settings, the cost–effectiveness of onabotulinumtoxinA was driven by a high incremental QALY gain while the cost–effectiveness for Urgent PC or Protect PNS was driven by low incremental costs with marginally higher incremental QALYs (Tables 3 & 4).

Table 2. Resource utilization, cost, and utility inputs for the original model and the updated model based on Medicare or commercial payer perspective.

Parameter	Original model Medicare	Updated model	
		Medicare	Commercial
Population and devices			
Age at baseline, years	60.4	60.4	60.4
Device life expectancy nonrechargeable SNS (Medtronic InterStim I or InterStim II)	7 [InterStim I]	4.4 [InterStim II]	4.4 [InterStim II]
Device life expectancy rechargeable SNS (Axonics r-SNM, InterStim Micro)	–	15	15
BSC inputs			
Cost of incontinence pads	Based on UIE rates	Based on UIE rates	Based on UIE rates
Patients on anticholinergics	23.9%	0%	0%
Oral drug monthly cost inputs			
Tolterodine ER 4 mg	\$208	\$335.82	\$335.82
Solifenacin 5 and 10 mg	\$274	\$262.60	\$262.60
Average, brand and generic anticholinergics	\$211	\$188.41	\$188.41
Average, generic anticholinergics only	\$211	\$100.05	\$100.05
Mirabegron 25 and 50 mg	\$282	\$431.74	\$431.74
Vibegron 75 mg	–	\$474.39	\$474.39
OnabotulinumtoxinA inputs			
Per injection cost	\$591	\$643	\$613
Administration, ambulatory clinic or physician office	\$311	\$398	\$486
Administration, ambulatory surgery	\$1605	\$968	\$1181
SNS inputs			
Cost of testing prior to SNS (PNE + stage 1) [†]	\$11,080	\$10,398	\$12,686
Cost of testing prior to SNS (PNE) [†]	\$3692	\$4883	\$5957
Cost of testing prior to SNS (stage 1) [†]	\$6980	\$5515	\$6729
Cost of the permanent implant	\$16,336	\$18,194	\$22,197
Physician visits for device programming	2 per year	2 per year	2 per year
Cost of additional physician visits for reprogramming	\$220	\$58	\$70
Cost of battery replacement	\$16,336	\$18,194	\$22,197
Cost of revision without replacement	\$1091	\$1981	\$2416
Cost of device explantation	\$16,336	\$18,194	\$22,197
Patients with success [‡] in OAB reduction	80% [Medtronic]	80% [Medtronic] 90% [Axonics]	80% [Medtronic] 90% [Axonics]
Patients with device-related adverse events	25% [Medtronic]	30% [Medtronic] 16.2% [Axonics]	30% [Medtronic] 16.2% [Axonics]
Patients on SNS receiving revision at 12 months	7.9% [Medtronic]	7.9% [Medtronic] 1% [Axonics]	7.9% [Medtronic] 1% [Axonics]
Patients on SNS with device explantation at 12 months	5% [Medtronic]	5% [Medtronic] 3.7% [Axonics]	5% [Medtronic] 3.7% [Axonics]
PTNS inputs			
Time (months) on PTNS procedure - PTNS	60	60	60
Probability of success at 3 months - PTNS	54.5%	54.5%	54.5%
Weekly cost of treatment (0–3 months)	\$1483	\$1566	\$1911
Monthly cost of treatment (3–6 months)	\$618	\$653	\$796
Monthly cost of treatment (>6 months)	\$371	\$392	\$478
Time (month) on PTNS procedure, Protect PNS	–	60	60
Probability of success at 3 months, Protect PNS	–	73.3%	73.3%
Cost of Protect PNS implant	–	\$3922	\$4785

[†] There are two different techniques for patient screening prior to SNS, percutaneous nerve evaluation (PNE) test and staged test: PNE testing involves placement of small percutaneous lead followed by test stimulations conducted over several days (PNE only), or alternatively it can involve a surgical procedure in two stages – the placement of a permanent lead for test stimulations followed by SNS device implantation upon success (stage 1); both techniques can be combined, where percutaneous lead and permanent lead are used prior to SNS implantation (PNE + stage 1); patient screening inputs did not change from the original model;

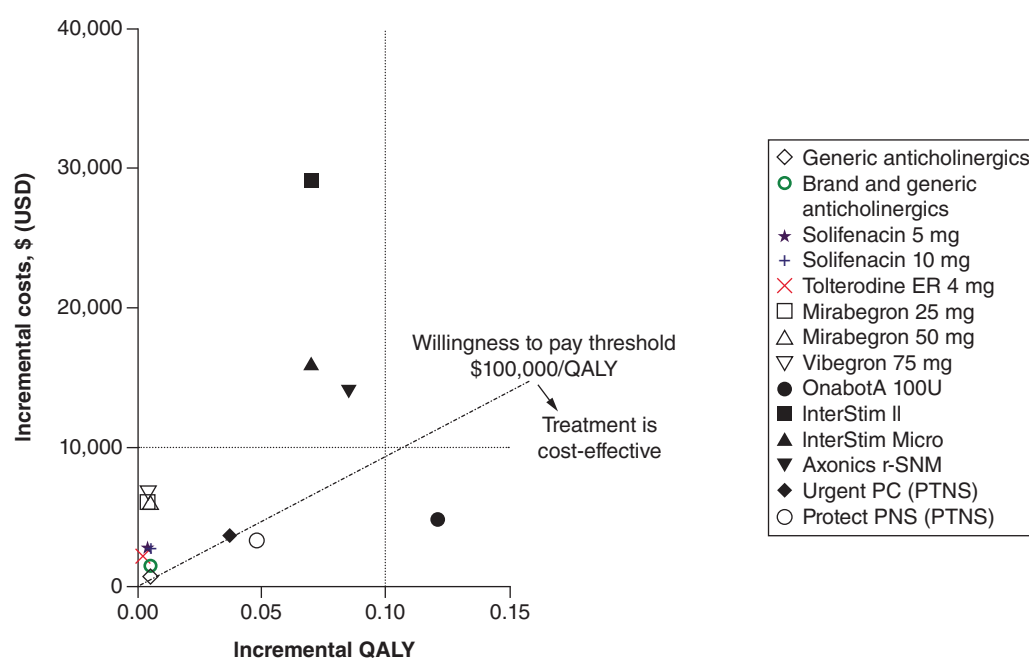
[‡] ≥50% improvement in urinary incontinence episodes, which was available from published SNS studies.

BSC: Best supportive care; PTNS: Percutaneous tibial nerve stimulation; r-SNM: Rechargeable sacral neuromodulation; SNS: Sacral nerve stimulation; UIE: Urinary incontinence episode.

Table 3. Base case-scenario at a 15-year time horizon, and 2- and 5-year ICERs (sensitivity analyses) using Medicare costs.

Study treatment	Total costs	Total QALYs	Incremental costs vs BSC	Incremental QALYs vs BSC	ICER per QALY gained (15 year)	ICER/QALY (2 year)	ICER/QALY (5 year)
BSC	\$18,018	9.535	–	–	–	–	–
Generic anticholinergics	\$18,745	9.539	\$728	0.005	\$158,866	\$158,889	\$158,867
Brand + generic anticholinergics	\$19,505	9.539	\$1487	0.005	\$324,658	\$324,704	\$324,658
Solifenacin 5 mg	\$20,795	9.538	\$2778	0.004	\$777,759	\$777,900	\$777,760
Solifenacin 10 mg	\$20,772	9.539	\$2754	0.005	\$601,269	\$601,354	\$601,270
Tolterodine ER 4 mg	\$20,194	9.536	\$2177	0.002	\$1,137,428	\$1,137,802	\$1,137,430
Mirabegron 25 mg	\$24,082	9.539	\$6065	0.004	\$1,466,559	\$1,469,053	\$1,466,691
Mirabegron 50 mg	\$24,066	9.539	\$6049	0.005	\$1,287,339	\$1,289,167	\$1,287,436
Vibegron 75 mg	\$24,691	9.539	\$6674	0.004	\$1,613,785	\$1,616,530	\$1,613,932
OnabotulinumtoxinA	\$22,810	9.656	\$4793	0.121	\$39,591	\$84,350	\$50,304
InterStim II	\$47,160	9.605	\$29,142	0.070	\$416,249	\$973,154	\$631,029
InterStim Micro	\$34,113	9.605	\$16,095	0.070	\$229,891	\$973,190	\$450,059
Axonics r-SNM	\$31,963	9.620	\$13,945	0.085	\$163,783	\$829,283	\$362,342
Urgent® PC (PTNS)	\$21,661	9.572	\$3643	0.037	\$98,031	\$123,260	\$98,031
Protect PNS (PTNS)	\$21,343	9.583	\$3326	0.048	\$69,027	\$130,669	\$69,027

BSC: Best supportive care; ER: Extended release; ICER: Incremental cost–effectiveness ratio; PTNS: Percutaneous tibial nerve stimulation; QALY: Quality-adjusted life-years; r-SNM: Rechargeable sacral neuromodulation.

**Figure 2.** Incremental cost–effectiveness plane using Medicare costs at 15-year time horizon.

OnabotA: OnabotulinumtoxinA; PTNS: Percutaneous tibial nerve stimulation; QALY: Quality-adjusted life-years.

Sensitivity analyses: 2- & 5-year time horizons

Based on Medicare costs, onabotulinumtoxinA remained the most cost-effective of all the OAB treatments evaluated vs BSC at a 2- and 5-year time horizon, with ICERs of \$84,350/QALY and \$50,304/QALY, respectively (Table 3). The β 3-adrenoceptor agonists were the least cost-effective OAB treatment vs BSC with ICERs > \$1,000,000/QALY at the 2- and 5-year horizons. The ICERs for the ‘brand and generic’ (\$324,704/QALY and \$324,658/QALY) and ‘generic only’ (\$158,889/QALY and \$158,867/QALY) anticholinergic arms at the 2- and 5-year time horizons

Table 4. Base-case scenario at a 15-year time horizon, and 2- and 5-year ICERs (sensitivity analyses) using commercial costs.

Study treatment	Total costs	Total QALYs	Incremental costs vs BSC	Incremental QALYs vs BSC	ICER per QALY gained (15 year)	ICER/QALY (2 year)	ICER/QALY (5 year)
BSC	\$20,410	9.535	–	–	–	–	–
Generic anticholinergics	\$21,125	9.539	\$715	0.005	\$156,070	\$156,092	\$156,070
Brand + generic anticholinergics	\$21,885	9.539	\$1474	0.005	\$321,862	\$321,907	\$321,862
Solifenacin 5 mg	\$23,178	9.538	\$2767	0.004	\$774,753	\$774,893	\$774,753
Solifenacin 10 mg	\$23,152	9.539	\$2742	0.005	\$598,473	\$598,557	\$598,473
Tolterodine ER 4 mg	\$22,580	9.536	\$2169	0.002	\$1,133,646	\$1,134,019	\$1,133,648
Mirabegron 25 mg	\$26,470	9.539	\$6059	0.004	\$1,465,232	\$1,467,725	\$1,465,365
Mirabegron 50 mg	\$26,452	9.539	\$6041	0.005	\$1,285,791	\$1,287,616	\$1,285,887
Vibegron 75 mg	\$27,079	9.539	\$6668	0.004	\$1,612,459	\$1,615,202	\$1,612,605
OnabotulinumtoxinA	\$25,526	9.656	\$5115	0.121	\$42,255	\$91,019	\$53,924
InterStim II	\$56,180	9.605	\$35,770	0.070	\$510,910	\$1,190,266	\$772,889
InterStim Micro	\$40,262	9.605	\$19,852	0.070	\$283,553	\$1,190,309	\$552,106
Axonics r-SNM	\$37,676	9.620	\$17,266	0.085	\$202,778	\$1,014,643	\$444,986
Urgent® PC (PTNS)	\$24,961	9.572	\$4551	0.037	\$122,446	\$153,229	\$122,446
Protect PNS (PTNS)	\$23,744	9.583	\$3334	0.048	\$69,200	\$130,842	\$69,200

BSC: Best supportive care; ER: Extended release; ICER: Incremental cost-effectiveness ratio; PTNS: Percutaneous tibial nerve stimulation; QALY: Quality-adjusted life-years; r-SNM: Rechargeable sacral neuromodulation.

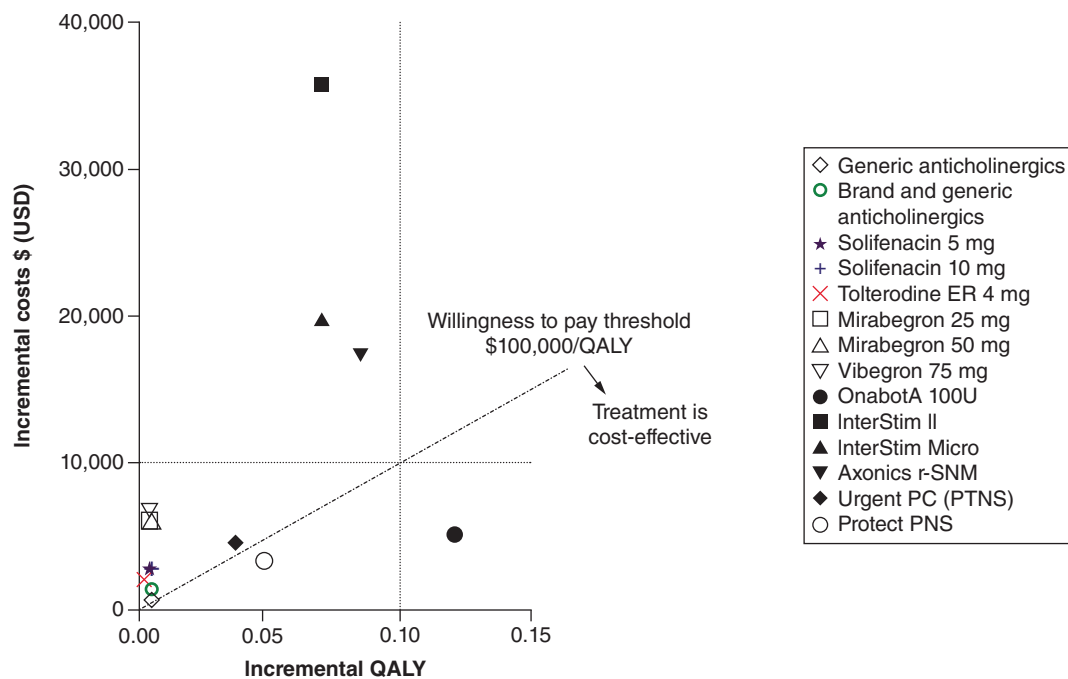


Figure 3. Incremental cost-effectiveness plane using commercial insurance costs at 15-year time horizon. OnabotA: OnabotulinumtoxinA; PTNS: Percutaneous tibial nerve stimulation; QALY: Quality-adjusted life-years.

were similar to those reported at the 15-year horizon. Compared with the 15-year horizon, the ICERs for the rechargeable SNS devices were two times greater at 5 years (r-SNM [\$362,342/QALY] and InterStim Micro [\$450,059/QALY]) and four to five times greater at 2 years (r-SNM [\$829,283/QALY] and InterStim Micro [\$973,190/QALY]). Urgent PC and Protect PNS were the only other cost-effective interventions at 5 years (\$98,031/QALY and \$69,027/QALY) and at 2 years (\$123,260/QALY and \$130,669/QALY), respectively.

OnabotulinumtoxinA was also the most cost-effective of all the evaluated OAB treatments over the 2- and 5-year time horizons when analyzed using commercial insurance costs with ICERs of \$91,019/QALY and \$53,924/QALY, respectively (Table 4). The β 3-adrenoceptor agonists were the least cost-effective OAB treatment vs BSC with ICERs >\$1,000,000/QALY at the 2- and 5-year horizons. The ICERs 'brand and generic' (\$321,907/QALY and \$321,862/QALY) and 'generic only' (\$156,092/QALY and \$156,070/QALY) anticholinergics at the 2- and 5-year time horizons were similar to those from a Medicare payer perspective. ICERs for the rechargeable SNS devices at 2 and 5 years were approximately 20% higher than those from a Medicare payer perspective. The only other treatment within the \$100,000/QALY cost-effectiveness threshold was Protect PNS (\$69,200/QALY) at the 5-year time horizon. Based on the higher threshold (\$150,000/QALY), Protect PNS was cost-effective at both 2 and 5 years, and Urgent PC was cost-effective at 5 years.

Discussion

The driving force behind the cost-effectiveness seen with onabotulinumtoxinA was a strong treatment response, as evidenced by the large difference in incremental QALYs vs BSC, while the cost-effectiveness seen with Protect PNS and Urgent PC was driven by low incremental costs. The low cost associated with generic anticholinergics was offset by negligible increases in incremental QALY vs BSC. Given that the QALY is calculated based on efficacy, discontinuation rates, and utility, it is feasible that the large difference in QALY was partly driven by lower discontinuation rates with onabotulinumtoxinA versus oral pharmacotherapies. The continued improvement in cost-effectiveness with onabotulinumtoxinA and SNS devices over time most likely reflects the sustained efficacy with onabotulinumtoxinA and factors in the proposed 15-year longevity of the newer SNS devices, respectively. Studies suggest that the time to request retreatment with onabotulinumtoxinA is approximately 7.5 months [21,44,45], and that efficacy following the first injection persists over multiple treatment cycles [21,46]. For Urgent PC and Protect PNS, treatment is assumed to last for 60 months/5 years, so ICERs were reduced after 5 years but were unchanged at the 15-year horizon despite having a relatively low cost. As such, any incremental improvement in treatment response with these neuromodulation therapies begins to diminish after 5 years. In the case of the oral pharmacotherapies, variations in the time horizon had a lesser impact due to the assumption of a high discontinuation rate at the end of 2 years (only 16% of patients still receiving any oral medication). Therefore, the ICERs vs BSC remain relatively constant over time because there are no additional costs or QALYs gained.

A prospective economic analysis of the Refractory Overactive Bladder: Sacral Neuromodulation vs BoTulinum Toxin Assessment (ROSETTA) randomized trial found higher costs for SNS (Interstim) at 2 years compared with onabotulinumtoxinA but similar QALYs and reductions in urgency UIEs/day [47]. Of note, the ROSETTA trial tested the earlier model of Interstim as well as onabotulinumtoxinA 200U, not the 100U FDA-approved dose evaluated here. Other previous OAB economic models using parameters specific to the Netherlands, UK, Spain, Italy and Canada suggested that SNS devices were more cost-effective than onabotulinumtoxinA [31,48–51]. Yet these models were limited by disparities in assumed treatment costs [48], inconsistencies in QALYs and stated assumptions [48], insufficient description of assumptions [49], conflicting conclusions after applying the stated assumptions [31,50], or failure to report specific cost or utility assumptions [51]. A detailed examination of these prior models was discussed previously [11], and one was retracted [31,52].

As with any cost-effectiveness model, assumptions were required to estimate outcomes, but our model used published literature when possible. Efficacy and discontinuation rates were based on clinical trial data, which may differ from real-world effectiveness and persistence rates. Furthermore, the use of clinical trial data was a limitation, particularly for the newer interventions for which limited short- and long-term data exist. Notably, efficacy data for Protect PNS were sourced from an early clinical trial with a very low sample size ($n = 30$). Another study limitation was the paucity of head-to-head studies comparing OAB treatments. Additionally, this analysis did not account for newer implantable devices that have recently been introduced, including eCoin[®] (Valencia Technologies, CA, USA), InterStim[™] X (Medtronic plc, MN, USA), and F15[™] (Axonics Modulation Technologies, CA, USA), which did not have data available at the time this study was conducted. In addition, non-responders were assumed to revert to BSC. Strengths of this study are that it reflects many of the currently available therapies in OAB and it incorporates the different payer perspectives in the US by analyzing cost-effectiveness from Medicare and commercial contexts.

It is important to recognize that cost and the influence of payers are among many factors that influence the choice of treatment in patients with OAB, and treatment should be individually tailored based on the patient's condition and treatment risks. Patient and disease characteristics that must be considered include age, lifestyle,

comorbidities, current medications and willingness to undergo invasive treatment. Furthermore, cost is not always measured in US dollars, and there will be country-specific differences to consider such as the role and influence of payers, the level of healthcare cost reimbursement, and the burden of out-of-pocket costs for the patient.

Conclusion

In this updated cost-effectiveness analysis, onabotulinumtoxinA remains the most cost-effective OAB treatment compared with BSC from a US payer perspective despite the inclusion of the new rechargeable neuromodulation devices for SNS (r-SNM, InterStim Micro) and PTNS (Protect PNS), vibegron, and the stratification of anticholinergics by cheaper generic and costlier brands. None of the oral pharmacotherapies (anticholinergics and β 3-adrenoceptor agonists) or rechargeable SNS devices were cost-effective compared to BSC. Protect PNS and Urgent PC were cost-effective although at higher ICERs than onabotulinumtoxinA versus BSC. The model results were unaffected by the varying assumptions assessed in sensitivity (2- and 5-year horizon) and the scenario analyses (Medicare vs commercial costs).

Summary points

- Overactive bladder is a prevalent and chronic condition associated with high health care costs and impaired quality of life.
- Understanding the cost-effectiveness of available treatment options for the management of overactive bladder has important implications to treatment decision-making in clinical practice and access considerations by US payers.
- The present study reports an updated cost-effectiveness analysis that evaluated current oral pharmacotherapies (anticholinergics [generic and branded], mirabegron, and vibegron), onabotulinumtoxinA, and neuromodulation devices (r-SNM, InterStim II, InterStim Micro, Urgent PC, Protect PNS) compared with best supportive care for the management of OAB from a Medicare and commercial payer perspective.
- Of the available treatment options examined in this study, onabotulinumtoxinA was the most cost-effective therapy for managing overactive bladder in patients who inadequately respond to or are intolerant of oral anticholinergic therapy. Protect PNS and Urgent PC were also cost-effective. Neither anticholinergics, β 3-adrenoceptor agonists, or rechargeable SNS devices were cost-effective compared with BSC.
- The cost-effectiveness results in the base case (15-year time horizon) were maintained across different time horizons (i.e., 2 and 5 years) and payer type (i.e., Medicare or commercial).

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: www.futuremedicine.com/doi/suppl/10.2217/cer-2022-0089

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Ethical conduct of research

Not applicable since the data are based on economic modeling using efficacy and safety inputs from previously published OAB studies.

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