Title

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Journal

Investigative urology, 203(5)

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Publication Date

2020-05-01

DOI

10.1097/JU.0000000000000656

Peer reviewed

HHS Public Access

Author manuscript

J Urol. Author manuscript; available in PMC 2020 May 07.

Published in final edited form as:

J Urol. 2020 May ; 203(5): 969–977. doi:10.1097/JU.0000000000000656.

Cost-Effectiveness of Sacral Neuromodulation versus OnabotulinumtoxinA for Refractory Urgency Urinary Incontinence: Results of the ROSETTA Randomized Trial

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Abstract

Purpose—Sacral neuromodulation and intradetrusor onabotulinumtoxinA injection are therapies for refractory urgency urinary incontinence. Sacral neuromodulation involves surgical implantation of a device that can last 4 to 6 years while onabotulinumtoxinA therapy involves serial office injections. We assessed the cost-effectiveness of 2-stage implantation sacral neuromodulation vs 200 units onabotulinumtoxinA for the treatment of urgency urinary incontinence.

Materials and Methods—Prospective economic evaluation was performed concurrent with the ROSETTA (Refractory Overactive Bladder: Sacral Neuromodulation vs. BoTulinum Toxin Assessment) randomized trial of 386 women with 6 or more urgency urinary incontinence episodes on a 3-day diary. Analysis is from the health care system perspective with primary within-trial analysis for 2 years and secondary 5-year decision analysis. Costs are in 2018 U.S. dollars. Effectiveness was measured in quality adjusted life-years (QALYs) and reductions in urgency urinary incontinence episodes per day. We generated incremental cost-effectiveness ratios and cost-effectiveness acceptability curves.

Results—Two-year costs were higher for sacral neuromodulation than for onabotulinumtoxinA ($35,680 [95% CI 33,920e37,440] vs $7,460 [95% CI 5,780e9,150], p <0.01), persisting through 5 years ($36,550 [95% CI 34,787e38,309] vs $12,020 [95% CI 10,330e13,700], p <0.01). At 2 years there were no differences in mean reduction in urgency urinary incontinence episodes per day (−3.00 [95% CI −3.38 e −2.62] vs −3.12 [95% CI −3.48 e −2.76], p[0.66) or QALYs (1.39 [95% CI 1.34e1.44] vs 1.41 [95% CI 1.36e1.45], p[0.60). The probability that sacral neuromodulation is cost-effective relative to onabotulinumtoxinA is less than 0.025 for all willingness to pay values below $580,000 per QALY at 2 years and $204,000 per QALY at 5 years.

Conclusions—Although both treatments were effective, the high cost of sacral neuromodulation is not good value for treating urgency urinary incontinence compared to 200 units onabotulinumtoxinA.

Keywords

urinary incontinence; urge; cost-benefit analysis; transcutaneous electric nerve stimulation; botulinum toxins; type A

Overactive bladder includes symptoms of urgency, frequency and urgency urinary incontinence and affects nearly 1 in 3 women.[1] This condition has a negative impact on quality of life, resulting in social isolation, depression, lower work productivity, poor sleep quality and decreased sexual satisfaction.[2–6] National costs of UUI have been estimated at $76.2 billion in 2015 with expected costs of $82.6 billion in 2020.[7] A recent systematic

review of overactive bladder specific costs estimated $656 to $860 per patient annually, with total health care costs 43% to 117% higher for patients with overactive bladder.[8] First line therapy involves behavior modification and fluid management followed by medical therapy, typically with anticholinergic or beta adrenergic medications.[9,10] For women with refractory UUI sacral neuromodulation and onabotulinumtoxinA are commonly used third line treatment strategies. However, these treatment modalities differ. SNM involves surgical implantation of the pulse generator device that may last 4 to 6 years. The BTX duration of effect is self-limited and involves repeated injections in the office at least annually. Few studies have evaluated the cost-effectiveness of these modalities[11–13] and trial based cost-effectiveness results of SNM vs BTX have not been reported.

The ROSETTA trial demonstrated that SNM and BTX have similar effectiveness through 2 years for women with UUI.[14] While these remain standard third line therapies, their economic implications have not been adequately assessed. Understanding the relative cost per improvement in health related quality of life may help patients, clinicians and payers make informed decisions about SNM or BTX when other therapies have failed. The objective of this planned secondary analysis was to assess the 2-year cost-effectiveness of SNM vs 200 units BTX and to model 5-year cost-effectiveness based on trial results.

MATERIALS AND METHODS

Trial Design and Patients

The ROSETTA trial included women with 6 or more UUI episodes on a 3-day diary for whom other therapies had failed and was conducted at 9 U.S. sites from July 2012 through February 2016.[14,15] Patients were randomized 1:1 to SNM or BTX stratified by site and age (younger than 65 years vs 65 or older). Institutional review board approval was received (IRB No. 814026).

Participants randomized to SNM underwent a 2-stage implantation procedure. Those who had a 50% or greater reduction in UUIEs after SNM lead placement were identified as clinical responders and received pulse generator placement. The SNM clinical responders could undergo device reprogramming and revisions but not additional UUI therapy before 6 months. Participants randomized to 200 units BTX who had a 50% or greater reduction in UUI episodes 1 month after the injection were identified as clinical responders and could receive up to 2 additional injections between 6 and 24 months. Nonresponders in both groups were allowed to use additional UUI therapies (eg medications). After 6 months nonresponders could receive the alternate therapy.

Economic Evaluation Design

A prospective cost-effectiveness analysis was conducted from the health care sector perspective to assess the incremental cost per quality adjusted life-year gained and the incremental cost per UUIE averted for SNM vs BTX. This approach conforms with the Second Panel on Cost-Effectiveness in Health and Medicine recommendation for a reference case analysis from the health care sector perspective[16] and the CHEERS health economic evaluation guidelines.[17] An intent to treat approach was used, including responders and

nonresponders. The primary analysis time frame was the 2-year trial duration. To conduct analysis for a 5-year horizon we modeled post-trial costs and outcomes through 5 years, the average SNM time to replacement. Costs were measured in 2018 U.S. dollars and assigned primarily from the 2018 Medicare Fee Schedule. Resource utilization data were from the February 2012 to January 2015 trial period. Costs and QALYs were estimated on a present value basis using an annual discount rate of 3%.

Effects

The primary effectiveness outcome was the 2-year QALY. Other effectiveness outcomes included 2-year change from baseline in mean daily UUI episodes, overactive bladder specific quality of life, patient satisfaction and symptom control.

QALYs were calculated from HUI-3 responses collected at baseline and at 6, 12 and 24 months (supplementary Appendix A, https://www.jurology.com).[18] To estimate 5-year QALYs, HUI-3 scores at 24 months were assumed to remain the same between 2 and 5 years.

Mean daily UUI episode was calculated from the 3-day diaries collected at baseline and 24 months (supplementary Appendix B, https://www.jurology.com). To estimate 5-year mean daily UUI episodes results at 24 months were assumed to remain the same between 2 and 5 years. The OAB-q SF (Overactive Bladder Questionnaire Short Form)[19,20] and the UDI-SF (Urinary Distress Inventory Short Form)[21] provided quality of life measures specific to overactive bladder. The OAB-SATq (Overactive Bladder Satisfaction with Treatment Questionnaire),[22] PGSC (Patient Global Symptom Control) and PGI-I (Patient Global Impression of Improvement)[23] assessed patient satisfaction and symptom control.

Costs

Health care sector costs incurred by payers and participants were included for therapies and UUI related health care. Utilization data collected during the trial were multiplied by national Medicare reimbursement rates or published prices to estimate costs for each participant event recorded. The data on number of UUI related procedures performed, adverse clinical events (eg UTIs) and other health care for UUI (eg medications, physical therapy) were collected at 1, 4, 6, 12 and 24 months. Unit costs were applied to calculate total costs per participant through 2 years (supplementary Appendix C, https://www.jurology.com).

For participants randomized to SNM the costs of lead placement, neurostimulator implantation, reprogramming and any lead removal or revisions or removals that occurred during the trial were included in analysis. For participants randomized to BTX the costs of the initial injection of 200 units BTX and reinjections within 2 years were included. SNM participants who received BTX also had cost included for each injection. BTX participants who received SNM also had cost included for SNM related services. Participants lost to followup were assumed to have no additional costs and this assumption was examined in sensitivity analysis (supplementary Appendix D, https://www.jurology.com).

To model costs for 2 through 5 years health care utilization was assumed to occur at the same rates as during the trial. For SNM participants treatment was conservatively assumed to include no reprogramming, revisions or removals. For BTX participants we assumed the same rate of injections as in the trial. We assumed SNM participants receiving BTX would continue using BTX and BTX participants receiving SNM would continue with SNM. The same utilization rates observed during the trial for each treatment were assumed for clinic visits, adverse events and OAB medications.[14,15]

Analysis

QALYs and change from baseline in UUI episodes per day were compared between groups using analysis of covariance with adjustment for baseline values (alternative approach in supplementary Appendix E, https://www.jurology.com). For all other measures the change from baseline was estimated using a repeated measures mixed linear model.

The primary cost-effectiveness measure was the 2-year incremental cost-effectiveness ratio, the difference between SNM and BTX in mean cost divided by difference in mean QALYs. A 2-year ICER was also calculated using UUI episodes as effectiveness (UUI episodes per day ICER).

Mean cost and mean QALY pairs for SNM and BTX were generated from 5,000 replications and plotted on the cost-effectiveness plane. Five-year uncertainty analysis assumed a gamma distribution for 5-year QALYs. ICER replications were compared to different levels of willingness to pay to determine the percentage of replications that would be cost-effective at values ranging from zero to $2 million per QALY gained.[24,25] Cost-effectiveness acceptability curves display these percentages. A similar approach was used for UUI episodes per day ICERs. SAS® version 9.4 was used for effectiveness and Stata® version 15.0 for cost and cost-effectiveness uncertainty analyses.

Threshold analyses were performed to identify the SNM device and procedure costs, impact of 1-stage vs 2-stage SNM implantation, length of SNM technology life, UTI treatment costs and frequency of BTX injections that would result in similar costs for each group.

RESULTS

Study Population and Interventions

The study population was described previously.[14,15] Figure 1 shows the 386 randomized participants followed for up to 2 years and 364 had baseline and at least 1 followup UUI episode measurement. Baseline characteristics were similar between groups (table 1). Overall 83.2% of participants were white, mean ± SD age was 63.0 ± 11.6 years, mean body mass index was 32.2 ± 8.2 kg/m^2 and mean UUI episodes per day was 5.3 ± 2.7. Of the SNM group 82% underwent pulse generator implantation, and during the trial 58% required reprogramming, 3% revisions and 8.6% removals. Of the BTX group 83% were clinical responders, and during the trial 72% of responders requested a second injection and 48% requested a third.

Outcomes and QALYs, 2 Years

Results for the 6-month intent to treat[15] and 2-year clinical responder populations[14] have been reported. QALYs were similar between the groups at 2 years at 1.39 (95% CI 1.34e1.44) for SNM and 1.41 (95% CI 1.36e1.45) for BTX (p[0.60, table 2). Mean number of UUI episodes per day declined for both groups but the reduction was not significantly different between groups (reduction of 3.00 [95% CI 2.62e3.38] for SNM vs 3.12 [95% CI 2.76e3.48] for BTX, p[0.66).

Condition specific symptom and quality of life outcomes improved in both groups, including in the OAB-q SF, PGI-I, UDI and IIQ (Incontinence Impact Questionnaire). However, changes were not different between groups except for the PGI-I bladder function subscale, where the BTX group reported greater improvement than the SNM group (table 2 and supplementary Appendix F, https://www.jurology.com).

Costs and Cost-Effectiveness

Table 2 shows estimated costs by treatment group and by type of cost. The cumulative mean per person cost over 2 years was $35,680 (95% CI 33,920e37,440) for the SNM group and $7,460 (95% CI 5,780e9,150) for the BTX group (p <0.01). The estimated cumulative mean per person cost through 5 years was $36,550 (95% CI 34,787e38,309) for SNM and $12,020 (95% CI 10,330e13,700) for BTX (p <0.01).

Because incremental costs per QALY gained were negative, SNM was dominated by BTX at 2 and 5 years. However, uncertainty analysis showed estimates in both upper quadrants of the cost-effectiveness plane, indicating higher mean costs of SNM but either higher or lower mean QALYs (fig. 2, A and table 3). Results were similar at 2 and 5 years. Cost-effectiveness acceptability curves show that the probability that SNM is cost-effective compared to BTX is less than 0.025 at 2 and 5 years for all willingness to pay values less than $582,850 per QALY and $204,220 per QALY, respectively (fig. 2, B). The incremental cost per reduction in UUI episodes was negative, suggesting SNM was dominated by BTX at 2 and 5 years (supplementary Appendix F, https://www.jurology.com).

Sensitivity Analysis

Threshold analysis showed that with a reduction in SNM costs of at least 69% at 2 years and 60% at 5 years, they would not differ from those of BTX. The majority of SNM costs are related to the device (40%) and implantation procedure (57%). A single stage implantation technique would reduce SNM costs by at least 15% compared to 2-stage, conservatively not including implantation and explantation costs for the trial's stage 1 nonresponders. The assumption of rechargeable SNM technology, but no other changes in costs, would result in similar costs for SNM and BTX by 39 years for 2-stage and 25 years for single stage implantation. Increasing the frequency of BTX injections to 6 per year from the observed average of 1 to 2 per year or assuming UTI antibiotics at $750 per infection would result in no difference in SNM and BTX costs at 5 years.

DISCUSSION

Cost-effectiveness comparison of 2-stage SNM vs 200 units BTX using within-trial data from a randomized, a controlled trial demonstrates that SNM is not a good value for UUI treatment compared to BTX. The probability that the ICER is less than or equal to the generally accepted maximum willingness to pay of approximately $150,000 per QALY gained is approximately 1%.[26]

To our knowledge this study is the first cost-effectiveness comparison of SNM vs BTX using within-trial data from a randomized, controlled trial. Model based analyses have evaluated the cost-effectiveness of SNM vs BTX for refractory UUI. In those studies QALY results were based on estimated utility scores rather than trial based measurements. Siddiqui et al developed a 2-year Markov model from the United States societal perspective comparing SNM and 200 units BTX, and found that SNM was not cost-effective compared to BTX for willingness to pay up to $100,000 per QALY.[11] Arlandis et al used a 10-year Markov model to perform a 3-way comparison of SNM, BTX and medication from the Spanish National Health Service perspective, showing that SNM was cost-effective compared to 100 units BTX using thresholds of €30,000 per QALY.[12] However, their model assumed better SNM outcomes and costs almost equal to 100 units BTX after 10 years, did not account for SNM reprogramming or revisions and assumed all neurostimulator replacements occurred at 7 years. Leong et al used a 5-year model to compare SNM to BTX from the Netherlands' societal perspective, and found that SNM was cost-effective at €40,000 per QALY at 4 years if both procedures were performed using general anesthesia, but not when BTX was performed using local anesthesia.[13]

In our randomized trial there were no significant differences in effectiveness between SNM and 200 units BTX across multiple effectiveness measures including QALYs, UUI episodes per day, and condition specific symptom and health related quality of life outcomes. In contrast, costs were significantly higher for SNM than BTX. Sensitivity analysis findings indicated how reduction of SNM device and implantation costs, limited need for SNM pulse generator replacement with rechargeable technology, increased BTX injection frequency or higher UTI treatment costs would impact cost-effectiveness. Findings indicated that single stage SNM implantation is not cost-effective at the current cost and rechargeable SNM technologies would need to last significantly longer than the 15-year testing to be cost-effective.

Strengths of this analysis include that cost-effectiveness data were obtained from a large, multicenter, randomized, controlled trial measuring utility scores and health related quality of life in women treated with SNM or BTX. Limitations were that QALYs, UUI episodes and costs for years 2 to 5 were estimated based on trial use and end point values for health related quality of life and bladder diaries. SNM reprogramming, revisions and removals were conservatively not included, which could underestimate costs for the SNM group. Another limitation is the length of followup to 2 years. A longer period would obtain BTX reinjection data and assess for potential decreased efficacy with multiple injections, dropout rates for SNM and BTX, crossover rates to the other therapy and the length of time before SNM neurostimulator replacement. Lastly, we were unable to account for full costs for 22

BTX participants. However, sensitivity analyses confirmed that censored BTX costs did not affect results (supplementary Appendix C, https://www.jurology.com).

The findings from this cost-effectiveness analysis cannot be extrapolated to other doses of BTX (100 or 150 units) and may not be generalizable to other populations, such as men with lower urinary tract symptoms, women with primarily urgency and frequency, or women with fecal and urinary incontinence.

CONCLUSIONS

Although SNM and BTX were effective therapies, the high cost of SNM in its current form is not a good value for treating refractory UUI compared to 200 units BTX at 2 or 5 years. A longer study would determine whether changes, such as increased frequency of BTX injections or reduction in SNM costs with new technology, would alter the cost landscape and the cost-effectiveness conclusions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

We thank the coordinators and all those who made this work possible (see Appendix).

Supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

APPENDIX

Coordinators included the following: University of Alabama, Julie E. Burge, BS, Kathy S. Carter, RN, BSN, Ryanne R. Johnson, BSN, RNC, WHNP-BC, CRNP, Jeannine McCormick, RN, BSN, MSN, CRNP, Robin R. Willingham, RN, BSN; Brown University, Ann Meers, Allegra Parrillo; University of California, San Diego/Kaiser San Diego/Kaiser Downey, Gisselle Zazueta-Damian, Nancy Flores; Cleveland Clinic, Andrea Aaby, BS, Ly Pung, RN; Duke University, Akira Hayes, MS, Nicole Longoria, PA-C, Shantae McLean, MPH, CCRC; Oregon Health Sciences University, Amanda Holland, MPH; University of New Mexico, Karen Taylor, BA, Julia Middendorf, RN; University of Pennsylvania, Michelle Kinglee; and University of Pittsburgh, Judy Gruss, RN, Karen Mislanovich, RN. Collaborators included the following: University of Alabama, R. Edward Varner, MD, Tracey S. Wilson, MD, Holly Richter, MD, PhD, Alayne D. Markland, DO; Brown University, Deborah L. Myers, MD; University of California, San Diego/Kaiser San Diego/Kaiser Downey, Shawn A. Menefee, MD; Cleveland Clinic, Bradley Gill, MD, Sandip Vasavada, MD; Duke University, Amie Kawasaki, MD, Nazema Y. Siddiqui, MD, Anthony G. Visco, MD, Alison C. Weidner, MD; Oregon Health Sciences University, W. Thomas Gregory, MD; University of New Mexico, Yuko Komesu, MD; University of Pennsylvania, Lily A. Arya, MD, Ariana L. Smith, MD; University of Pittsburgh, Michael Bonidie, MD, Christopher Chermansky, MD, Pamela Moalli, PhD, MD, Jonathan Shepherd, MD, Gary Sutkin, MD, Halina Zyczynski, MD; Northwest Texas Physician Group, Amarillo, TX, Susan F. Meikle, MD; RTI International, Katrina Burson, Allyson Drew, Marie Gantz, PhD,

Kendra Glass, Carolyn Huitema, Emily Honeycutt, MS, Amy Kendrick, Tracy L. Nolen, James Pickett, Amanda Shaffer, Yan Tang, Dennis Wallace, Ryan E. Whitworth, Kevin A. Wilson. Data Safety Monitoring Board: Kay Dickersin, Johns Hopkins Bloomberg School of Public Health, Luohua Jiang, Texas A&M Health Science University, Missy Lavender, Women's Health Foundation, Kate O'Dell, UMass Memorial Medical Center, Kate Ryan, National Women's Health Network, Paul Tulikangas, University of Connecticut Hartford Hospital, Lan Kong, Penn State University College of Medicine, Donna McClish, Virginia Commonwealth University, Leslie Rickey, Yale New Haven Hospital, David Shade, The Johns Hopkins University, Ashok Tuteja, University of Utah, Susan Yount, Frontier Nursing University, Lexington, KY.

Abbreviations and Acronyms

BTX	onabotulinumtoxinA
HUI-3	Health Utilities Index Mark 3
ICER	incremental cost-effectiveness ratio
OAB	overactive bladder
QALY	quality adjusted life-year
ROSETTA	Refractory Overactive Bladder: Sacral Neuromodulation vs BoTulinum Toxin Assessment
SNM	sacral neuromodulation
UTI	urinary tract infection
UUI	urgency urinary incontinence
UUIE	UUI episode

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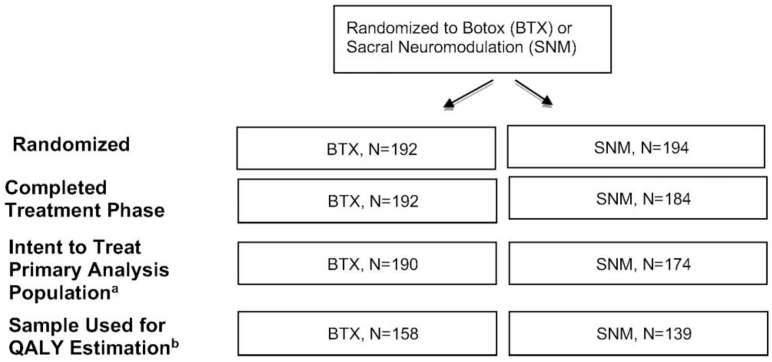

Figure 1.

Flow diagram of randomized participants and effectiveness questionnaire respondents. a, includes intent to treat primary analysis population used for 6-month ROSETTA results.[15] Population was limited to subjects who completed treatment and had baseline and at least 1 followup UUIE diary. b, limited to subjects with at least 1 baseline and 1 followup HUI-3 measurement, minimum data required to implement repeated measures mixed linear model to estimate QALYs.

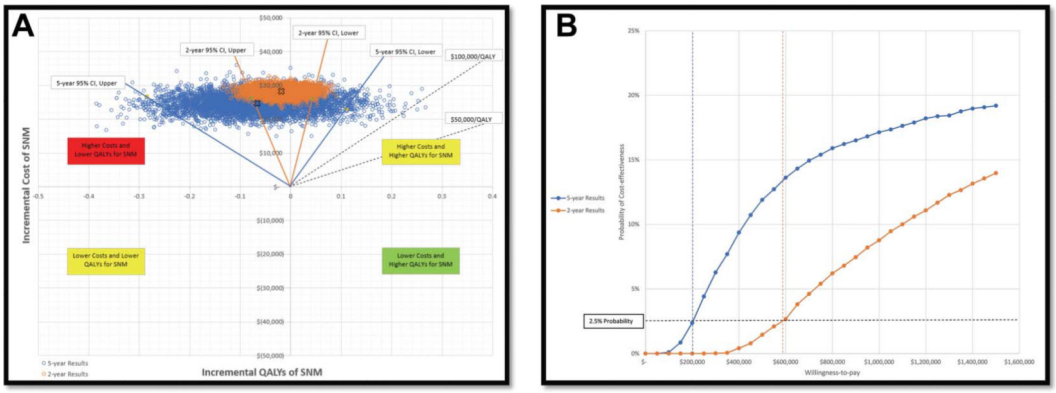

Figure 2.

ICER scatterplot (A) and cost-effectiveness acceptability curve (B) for SNM vs BTX for 2 and 5-year estimates. A, scatterplot of points representing pairs of mean differences in cost and mean differences in QALYs for SNM vs BTX using 2 and 5-year analysis horizons. All points from 5,000 replications for both time horizons lie above horizontal axis, indicating that SNM is expected to always be more costly than BTX. Points to right of vertical axis represent replications in which SNM was more effective than BTX, while points on left indicate replications in which BTX was more effective than SNM. X points indicate ICER point estimates. B, cost-effectiveness acceptability curves for SNM vs BTX for 2 and 5-year analysis horizons. For willingness to pay of $580,000 per QALY gained over 2 years, SNM had 2.5% probability of being cost-effective vs BTX. For willingness to pay of $204,000 per QALY gained over 5 years, SNM had 2.5% probability of being cost-effective vs BTX.

Table 1.

Baseline characteristics of participants

	SNM Group (174)	BTX Group (190)
Mean age (SD)	63.1 (11.8)	62.9 (11.5)
No. Hispanic ethnicity (%) [*,†]	10 (5.9)	18 (9.7)
No. race (%): [†]		
White	149 (85.6)	154 (81.1)
Black	16 (9.2)	22 (11.6)
Other	9 (5.2)	14 (7.4)
Mean kg/m^2 body mass index (SD) [‡]	31.7 (7.5)	32.6 (8.7)
No. history of recurrent UTIs (%)	25 (14.4)	24 (12.6)
Mean UUIEs/day (SD) [§]	5.19 (2.68)	5.39 (2.66)
Mean HUI-3 score (SD) [//]	0.74 (0.28)	0.71 (0.30)
Mean OAB-q SF symptom bother score (SD) [¶]	76.1 (16.8)	74.6 (19.5)
Mean OAB-q SF quality of life score (SD) [**]	36.8 (21.6)	38.2 (23.0)
Mean UDI-SF score (SD)	59.2 (16.9)	60.9 (18.3)
Mean IIQ score (SD) [††]	52.5 (25.8)	52.7 (27.6)

None of baseline values demonstrated differences between treatment groups at $p < 0.05$.

[*] SNM 170 responses, BTX 185 responses.

[†] Self-reported.

[‡] BTX 189 responses.

[§] Calculated from patient reported 3-day diary entries.

[//] SNM 155 responses, BTX 169 responses.

[¶] SNM 172 responses.

[**] SNM 173 responses.

[††] BTX 189 responses.

J Urol. Author manuscript; available in PMC 2020 May 07.

Table 2.

Effectiveness and costs by treatment group

Measure	SNM (174)	BTX (190)	Difference between SNM vs BTX (95% CI)	p Value
Adjusted mean effectiveness (95% CI):				
QALY (2-yr) *	1.39 (1.34, 1.44)	1.41 (1.36, 1.45)	−0.02 (−0.09, 0.05)	0.60
QALY (5-yr) *	3.24 (3.09, 3.39)	3.31 (3.16, 3.46)	−0.07 (−0.28, 0.14)	0.49
UUIE/day reduction from baseline †	3.00 (2.62, 3.38)	3.12 (2.76, 3.48)	−0.12 (−0.64, 0.41)	0.66
HUI-3 change from baseline ‡	−0.04 (−0.08, 0.003)	−0.03 (−0.07, 0.01)	−0.01 (−0.06, 0.05)	0.83
Mean 2-Yr costs (SD): §,‖				
SNM ¶	34,760 (11,980)	3,950 (11,900)	30,810 (28,340; 33,270)	<0.001
BTX **	170 (550)	2,620 (1,140)	−2,450 (−2,260; −2,640)	<0.001
Clinic visits ††	350 (230)	400 (190)	−50 (−7, −90)	0.02
Adverse events ‡‡	330 (620)	450 (460)	−120 (−8, −230)	0.03
Other §§	80 (220)	50 (130)	30 (−3, 70)	0.07
Mean 2-Yr cost subtotal (95% CI)	35,680 (33,920; 37,440)	7,460 (5,780; 9,150)	28,220 (30,650; 25,790)	<0.001
Mean 2–5-Yr estimated costs: §,‖,‖‖				
SNM	180	20	160	Not applicable
BTX	240	3,980	−3,740	Not applicable
Clinic visits	450	520	−80	Not applicable
Adverse events	60	320	−260	Not applicable
2–5-Yr subtotal	870	4,560	−3,690	Not applicable
0–5-Yr mean cost (95% CI)	36,550 (34,787; 38,309)	12,020 (10,330; 13,700)	24,530 (22,100; 26,960)	<0.001

* SNM 134 responses, BTX 150 responses. Two-year QALYs calculated as described in Methods section using HUI-3 from baseline, 6, 12, and 24 months. Five-year QALY estimates summed 2-year QALYs and 2 through 5-year QALY estimates, which were extrapolated from 2-year HUI-3 estimates. Estimates and p values comparing groups are from analysis of covariance with adjustment for baseline HUI-3. QALYs were discounted using 3% discount rate.

† p values comparing groups are from analysis of covariance with missing data replaced by last observation carried forward and adjustment for baseline value.

‡ SNM 139 responses, BTX 158 responses. Estimates and p values comparing groups are from repeated measures mixed linear model.

§ All costs reported in 2018 U.S. dollars. Costs after first year were discounted using a 3% discount rate. Cost estimates higher than $10 were rounded to the nearest $10 increment.

‖ Mean costs compared between treatment groups using t-test.

[¶] Included all SNM responder and nonresponder SNM costs and BTX nonresponders who chose to receive SNM after 6 months. Majority of SNM costs were related to the device (40%) and implantation procedure (57%).

[**] Included all BTX responder and nonresponder BTX costs and SNM nonresponders who chose to receive BTX after 6 months.

[††] Included regular study visits conducted as part of trial and additional nonstudy visits.

[‡‡] Included UTIs (symptomatic, with or without positive culture, 104 in BTX and 62 in SMN) and need for clean intermittent catheterization after BTX (post-void residual greater than 300ml or greater than 200 ml with associated moderate to severe voiding bother, 45 in BTX). There was 1 hospital admission related to study interventions for SNM postoperative pain.

[§§] Included other treatments such as OAB medications, physical therapy and percutaneous tibial nerve stimulation.

[////] Estimated costs for years 2 to 5 were calculated as constant unit cost per treatment group. SNM treatment costs for 2 to 5 years conservatively assumed no reprogramming, reinsertion or removal costs. BTX injections were assumed to occur at same mean rate as observed during 2-year trial period, resulting in per year average of 1 additional injection for years 2 through 5 for the BTX arm, and 0.6 per year for individuals in SNM arm who had received BTX in years 1 and 2. Clinic visits for 2 to 5-year period were based on rate of visits observed during 2-year trial period. Adverse events included office visits for adverse events, UTI costs and self-catheterization costs, all assumed to occur at same rate per therapy group as in trial. “Other” costs were assumed to be $0. Clinic visit cost analysis assumed the continued use through 5 years of OAB medications reported during trial period and no additional physical therapy or percutaneous tibial nerve stimulation sessions in years 2 through 5.

Table 3.

Cost-effectiveness of SNM versus BTX, 2-year and 5-year estimates

ICER Measure, Time Horizon	ICER, SNM vs BTX (95% CI)
Incremental cost per QALY gained, 2-yr	Dominated by BTX ($582,850 or greater/QALY [upper right quadrant];-$344,160 or less/QALY [upper left quadrant])
Incremental cost per QALY gained, 5-yr	Dominated by BTX ($204,220 or greater/QALY [upper right quadrant];-$93,670 or less/QALY [upper left quadrant])
Incremental cost per reduction in UUIE/person/day, 2-yr	Dominated by BTX ($68,800 or greater/UUIE [upper right quadrant];-$43,390 or less/UUIE [upper left quadrant])
Incremental cost per reduction in UUIE/person/day, 5-yr	Dominated by BTX ($61,980 or greater/UUIE [upper right quadrant];-$37,350 or less/UUIE [upper left quadrant])

Primary cost-effectiveness measure was 2-year ICER of difference in 2-year mean cost of SNM vs BTX to difference in 2-year mean QALYs for SNM vs BTX in 2018 U.S. dollars. Two-year ICER was also calculated using UUIEs as effectiveness measure. Denominator of these ICERs was difference in mean change from baseline to 2 years for SNM vs BTX. For 5-year ICERs, HUI-3 and UUIEs were assumed to remain constant at 2-year values through 5 years. CIs were determined by bootstrap (fig. 2).