Sacral neuromodulation versus onabotulinumtoxinA for refractory urgency urinary incontinence: impact on fecal incontinence symptoms and sexual function

Uduak U. Andy, MD; Cindy L. Amundsen, MD; Emily Honeycutt; Alayne D. Markland, DO, MSc; Gena Dunivan, MD; Keisha Y. Dyer, MD, MPH; Nicole B. Korbly, MD; Megan Bradley, MD; Sandip Vasavada, MD; Donna Mazloomdoost, MD, FACOG; Sonia Thomas, DrPH; on behalf of the NICHD Pelvic Floor Disorders Network

BACKGROUND: Women with refractory urgency urinary incontinence can be treated with onabotulinumtoxinA or sacral neuromodulation. Little data exists on the comparative effects of treatment of refractory urgency urinary incontinence on other pelvic floor complaints, such as bowel and sexual function.

OBJECTIVE: The objective of this study was to compare the impact of these treatments on fecal incontinence and sexual symptoms.

METHODS: This was a planned supplemental analysis of a randomized trial in women with refractory urgency urinary incontinence treated with onabotulinumtoxinA (n = 190) or sacral neuromodulation (n = 174). Fecal incontinence and sexual symptoms were assessed at baseline and at 6, 12, and 24 months. Fecal incontinence symptoms were measured using the St Mark's (Vaizey) Fecal Incontinence severity scale. Sexual symptoms were measured using the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire-12 (PISQ-12) and the Pelvic Organ Prolapse/Incontinence Sexual Questionnaire, IUGA-Revised (PISQ-IR). The PISQ-IR allows measurement of sexual symptoms in both sexually active and non—sexually active adults. Primary outcomes were change in Vaizey and PISQ-12 scores between baseline and 6 months. Secondary outcomes were change in PISQ-IR total and subscores between baseline and 6 months and change in Vaizey, PISQ-12, and PISQ-IR scores between baseline and 12 and 24 months. Intent-to-treat analysis was performed using repeated measures mixed model to estimate change in all parameters from baseline while adjusting for the baseline score. A subgroup analysis of women with clinically significant bowel symptoms was conducted based on baseline Vaizey score of ≥12.

RESULTS: At baseline, mean Vaizey scores were indicative of mild fecal incontinence symptoms and were not different between onabotulinumtoxinA and sacral neuromodulation groups (7.6 ± 5.3 vs 6.6 ± 4.9, $P = .07$). The proportion of sexually active women (56% vs 63%, $P = .25$), mean PISQ-12 score (33.4 ± 7.5 vs 32.7 ± 6.7, $P = .55$), or PISQ-IR subscores were also not different between the onabotulinumtoxinA and sacral neuromodulation groups at baseline. There was no difference between women treated with onabotulinumtoxinA and those treated with sacral neuromodulation at 6 months in terms of improvement in fecal incontinence symptom score (Vaizey: -1.9, 95% confidence interval -2.6 to -1.2 vs -0.9, 95% confidence interval -1.7 to -0.2, $P = .07$) or sexual symptoms score (PISQ-12: 2.2, 95% confidence interval 0.7 to 3.7 vs 2.2, 95% confidence interval 0.7 to 3.7, $P = .99$). There was no difference in improvement between groups in the sexual symptom subscores in sexually active and non—sexually active women at 6 months. Similar findings were noted at 12 and 24 months. In a subgroup (onabotulinumtoxinA = 33 and sacral neuromodulation = 22) with clinically significant fecal incontinence at baseline (Vaizey score ≥12), there was a clinically meaningful improvement in symptoms in both groups from baseline to 6 months, with no difference in improvement between the onabotulinumtoxinA and sacral neuromodulation groups (-5.1, 95% confidence interval -7.3 to -2.8 vs -5.6, 95% confidence interval -8.5 to -2.6, $P = .8$).

CONCLUSION: There were no differences in improvement of fecal incontinence and sexual symptoms in women with urgency urinary incontinence treated with onabotulinumtoxinA or sacral neuromodulation. Women with significant fecal incontinence symptoms at baseline had clinically important improvement in symptoms, with no difference between the treatments. Our findings can help clinicians counseling women considering treatment for refractory urgency urinary incontinence.

Key words: botox, fecal incontinence, neuromodulation, sexual function, urinary incontinence, women

Pelvic floor disorders, which include urinary incontinence and fecal incontinence (FI), are common, with 25% of women in the United States reporting at least 1 disorder.[1] Women with pelvic floor disorders report worse sexual function, especially when associated with urinary incontinence.[2] A growing body of literature suggests that treatment for 1 pelvic floor disorder may positively impact other pelvic floor complaints, including sexual dysfunction. Recent work demonstrated that sacral neuromodulation (SNM) for the treatment of FI may improve other pelvic floor complaints, including urinary and sexual issues.[3] Additionally, the use of onabotulinumtoxinA (BTX) for the treatment of overactive bladder also demonstrated improvement in sexual function in a small study.[4] Given the common coexistence of pelvic floor disorders, studies that investigate the impact of treatment of 1 condition on other pelvic floor symptoms are needed.

Little data exists on the comparative effects of treatment of refractory urgency urinary incontinence (UUI) on other pelvic floor complaints, such as bowel and sexual function. The ROSETTA trial, a randomized trial comparing BTX vs SNM for treatment of refractory UUI in women,[5] was an ideal group to comparatively assess the impact of treatment of refractory UUI on global pelvic

Cite this article as: Andy UU, Amundsen CL, Honeycutt E, et al. Sacral neuromodulation versus onabotulinumtoxinA for refractory urgency urinary incontinence: impact on fecal incontinence symptoms and sexual function. Am J Obstet Gynecol 2019;221:513.e1-15.

0002-9378/$36.00

https://doi.org/10.1016/j.ajog.2019.06.018

AJOG at a Glance

Why was this study conducted?

This study compares bowel and sexual function outcomes in women seeking treatment for refractory urgency urinary incontinence and who were randomized to either onabotulinumtoxinA or sacral neuromodulation.

Key findings

There were no differences in improvement of fecal incontinence and sexual symptoms between the 2 treatments. Women with clinically significant fecal incontinence symptoms (Vaizey score ≥12) at baseline had clinically meaningful improvement in fecal incontinence symptoms after either treatment.

What does this add to what is known?

Our findings add to the limited evidence on how treatment for refractory urgency urinary incontinence affects other pelvic floor disorders such as bowel and sexual function. Further, our findings can help clinicians when counseling women considering either onabotulinumtoxinA or sacral neuromodulation for refractory urgency urinary incontinence and highlights that women with concomitant bothersome fecal incontinence symptoms can expect improvement when undergoing either treatment for refractory urgency urinary incontinence.

floor function. The primary objective of this planned supplemental analysis was to compare the impact of these treatments for refractory UUI on FI and sexual symptoms.

Materials and Methods

The ROSETTA trial was an open-label, randomized trial conducted at 9 sites participating in the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development—sponsored Pelvic Floor Disorders Network. The study design and methods have been previously published.[5] Women with refractory UUI who experienced ≥6 UUI episodes on a 3-day diary and failed behavioral interventions, physical therapy, and 2 medications were invited to participate. Women with neurologic disease, postvoid residual >150 mL, previous treatment with either study intervention, or ≥stage 3 prolapse were excluded. All sites received institutional review board approval, and all participants gave written informed consent (Clinicaltrials.gov NCT01502956).

Participants were randomized 1:1 to undergo SNM (InterStim, Medtronic, Dublin, Ireland) or to receive 200 U of BTX (Botox A, Allergan, Dublin, Ireland), and were stratified by clinical site and age group (<65 vs ≥65 years). SNM participants who demonstrated ≥50% reduction in UUI episodes on a bladder diary following stage I lead placement and proceeded to undergo stage II pulse generator placement were considered SNM clinical responders. BTX participants with ≥50% reduction in UUI episodes on a bladder diary 1 month following injection were considered BTX clinical responders. Nonresponders to SNM were allowed medication and could receive BTX therapy after 6 months. Nonresponders to BTX were allowed medication and could receive SNM therapy after 6 months. Between 6 and 24 months, responders to BTX could receive 2 additional injections performed a minimum of 4 months apart.

For this planned supplementary analysis, FI and sexual symptoms were measured at baseline and at 6, 12, and 24 months. Data were collected, via telephone, by research staff masked to the subjects' randomized group assignment. FI symptoms were measured using the St Mark's (Vaizey) Fecal Incontinence severity scale. The Vaizey scale has 7 items and assesses for frequency of incontinence of solid stool, liquid stool, and gas, as well as alterations in lifestyle secondary to FI, need to wear a pad or plug, use of constipating medication, and an assessment of fecal urgency. Total scores range from 0 (perfect continence) to 24 (totally incontinent).[6,7] The St. Mark's score was chosen to assess FI based on National Institutes of Health and Cochrane instrument recommendations and availability of robust data that correlate change in Vaizey score with change in FI episodes and data that the score is responsive to change.[8–10] The Vaizey score has been used extensively in the literature, including in ongoing FI treatment studies by our group,[11] which will allow for comparison of treatment effects across studies. Sexual symptoms were measured using the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire Short Form (PISQ-12) and the Pelvic Organ Prolapse/Incontinence Sexual Questionnaire, IUGA-Revised (PISQ-IR).[12,13] The PISQ-12 total score ranges from 0 to 48, with higher scores indicating better sexual function. The PISQ-12 was administered only if the participant indicated sexual activity in the past 6 months. The PISQ-IR measures sexual function for both sexually active and non—sexually active women. It allows calculation of a total score and subscores for sexually active women in 6 areas: Arousal, Orgasm (SA-AO); Partner Related (SA-PR); Condition Specific (SA-CS); Global Quality Rating (SA-GQR); Condition Impact (SA-CI); and Desire (SA-D). Subscores for women not sexually active (NSA) are calculated in 4 areas: Partner Related (NSA-PR); Condition Specific (NSA-CS); Global Quality Rating (NSA-GQR), and Condition Impact (NSA-CI). Each individual subscore ranges from 1 to 5, with higher score indicating better sexual function. The minimum important difference (MID) is the smallest change in score on patient-reported questionnaire that patients would perceive as clinically meaningful improvement. The MID for the Vaizey scale is 5.0.[7] The MID for the PISQ-12 and PISQ-IR scales have not been published. In the absence of a published MID, a distribution-based determination of the MID designates a change of 0.20 standard deviation (SD) as a "small" effect and 0.5 SD as a "medium" effect size for patient-reported questionnaires.[14]

The primary outcomes for this supplementary analysis were change in Vaizey and PISQ-12 scores between

baseline and 6 months. Secondary outcomes included change in PISQ-IR total and subscores between baseline and 6 months and change in Vaizey, PISQ-12, and PISQ-IR total and subscores between baseline and 12 and 24 months.

Intent-to-treat (ITT) analysis was performed using repeated measures mixed model to estimate change in all parameters from baseline while adjusting for the baseline score. A subgroup analysis of women with more severe bowel symptoms, defined as baseline Vaizey score ≥12, was performed.

The modified ITT population, used for the primary analysis, consisted of all randomized participants who initiated treatment and provided at least 1 postbaseline bladder diary assessment, as reported previously.[15,16] A planned secondary analysis was based on clinical responders, defined as participants with a 50% or more initial reduction in mean episodes of UUI in both treatment groups, and full device implantation in the SNM group.

Treatment groups were compared for mean change from baseline scores using a linear mixed model to account for missing data owing to missed visits and early discontinuations, with month (6, 12, and 24) as the unit of analysis and monthly change from baseline as the outcome. The model had terms for baseline value, treatment group, month category, treatment by month interaction, age group (<65 vs ≥65 years), and site consistent with randomization strata. Participant was treated as a random effect to account for within-person correlation. The model generated adjusted estimates of change from baseline by treatment group at the 3 time periods; F test *P* values at each time assessed the hypothesis that the mean change from baseline differed between treatment groups, and *t* test *P* values assessed whether the adjusted mean change in score from baseline differed from zero. The primary ITT comparisons for Vaizey and PISQ-12 score change at month 6 relative to baseline were each evaluated for statistical significance relative to $P < .05$. There was no adjustment for multiple primary outcomes because the bowel and sexual symptoms were considered separate domains. All other analyses are considered descriptive in nature, with no adjustment for multiple testing, and *P* values should be interpreted accordingly. A preplanned subgroup analysis of the Vaizey score was based on Vaizey baseline score ≥12 and <12. The interaction between baseline Vaizey score and treatment group at 6 months was assessed within the linear mixed model. All *P* values are based on 2-sided tests. Analyses were performed using SAS Version 9.4 (SAS Institute, Inc, Cary, North Carolina).

Results

As has previously been reported, 386 women were randomized to BTX (n = 194) or SNM (n = 192). Women with baseline and at least 1 postbaseline incontinence diary data were included in the ITT analysis (BTX = 190 and SNM = 174). Eighty-nine percent of women completed the 24-month follow-up (166 in BTX and 162 in SNM). Women with at least 50% reduction in UUI episodes were included in the clinical responder population (BTX = 159 and SNM = 139).[16] Baseline demographics and clinical characteristics were not different between the 2 groups (Table 1; Appendix: Clinical responder results). The average age was 63.0 ± 11.6, 85% were postmenopausal, and the majority were white. Participants had an average of 5.3 UUI episodes per day at baseline (Table 1).

Fecal incontinence symptoms

Mean baseline Vaizey scores were indicative of mild FI symptoms and were not different between women randomized to BTX vs SNM (7.6 ± 5.3 vs 6.6 ± 4.9, $P = .07$) (Table 1). Only 10 of the 364 women had a Vaizey score of 0 at baseline. At 6 months, there was statistically significant improvement from baseline in the Vaizey score in both the BTX and SNM groups, which was not significantly different between groups (-1.9, 95% confidence interval [CI] -2.6 to -1.2 vs -0.9, 95% CI -1.7 to -0.2, $P = .07$) but was less than the MID of 5.0.[7] The results were similar at 12 and 24 months with the exception that at 24 months, the improvement in Vaizey scores was attenuated (-0.6, 95% CI -1.3 to 0.1) in the SNM group (Table 2). Similar results were noted in the clinical responder analysis (Appendix).

The subgroup of women (n = 55) with baseline Vaizey scores ≥12 had clinically and statistically significant improvement from baseline at 6 months in both the BTX and SNM groups (-5.1, 95% CI -7.3 to -2.8 and -5.6, 95% CI -8.5 to -2.6), with no difference between groups ($P = .8$). The change in Vaizey score remained different from baseline in both groups at 12 and 24 months (Table 3, Figure).

In the subgroup (n = 234) with Vaizey scores <12, women in the BTX group had greater improvement in Vaizey score from baseline to 6 months compared to the SNM group (-1.0, 95% CI -1.8 to -0.3 vs 0.2, 95% CI -0.5 to 1.0, $P = .01$); however, the clinical significance of this small difference is not clear, and this difference was no longer present at 12 and 24 months (Table 3, Figure).

Sexual symptoms

At baseline, 56% and 63% of women who completed the PISQ-12 reported being sexually active in the past 6 months in the BTX and SNM groups, respectively ($P = .25$). Mean baseline PISQ-12 scores were reflective of the presence of poor sexual function[8] and did not differ between groups (33.4 ± 7.5 vs 32.7 ± 6.7, $P = .55$). Of those who reported sexual activity at baseline, 1 patient in the BTX group and 3 patients in the SNM group reported becoming non−sexually active at 6 months. Of those who reported being non−sexually active at baseline, 1 in each group reported sexual activity at 6 months. There was a statistically significant improvement in PISQ-12 score in both the BTX and SNM groups (2.2, 95% CI 0.7 to 3.7 and 2.2, 95% CI 0.7 to 3.7), corresponding to a "small" improvement in effect size. There was no difference between groups (P*p* = .99). The effects waned but a similar trend was noted at 12 and 24 months, which was only statistically significant in the BTX group (Table 2).

There were no differences between groups in the total PISQ-IR score or any

TABLE 1
Demographic and baseline characteristics for intention-to-treat population

Characteristic	Statistic/category	Treatment group		Total (n = 364)
		BTX (n = 190)	SNM (n = 174)	
Race	White	154 (81%)	149 (86%)	303 (83%)
	Black/African American	22 (12%)	16 (9%)	38 (10%)
	American Indian/ Alaskan Native	4 (2%)	1 (1%)	5 (1%)
	Asian	1 (1%)	1 (1%)	2 (1%)
	Other	6 (3%)	4 (2%)	10 (3%)
	More than 1 race	1 (1%)	2 (1%)	3 (1%)
	Unknown/not reported	2 (1%)	1 (1%)	3 (1%)
Ethnicity	Hispanic/Latina	18 (9%)	10 (6%)	28 (8%)
	Not Hispanic/Latina	167 (88%)	160 (92%)	327 (90%)
	Unknown/not reported	5 (3%)	4 (2%)	9 (2%)
Age at baseline (years)	Mean (SD)	62.9 (11.5)	63.1 (11.8)	63.0 (11.6)
BMI (kg/m^2)	Mean (SD) [n]	32.6 (8.7) [189]	31.7 (7.5)	32.2 (8.2)
Functional comorbidity index	Mean (SD)	3.8 (2.3)	3.6 (2.3)	3.7 (2.3)
Current smoker	No	168 (88%)	156 (90%)	324 (89%)
	Yes	22 (12%)	18 (10%)	40 (11%)
Menopausal status	Postmenopausal	162 (85%)	149 (86%)	311 (85%)
	Premenopausal	20 (11%)	18 (10%)	38 (10%)
	Not sure	8 (4%)	7 (4%)	15 (4%)
Mean urge urinary incontinence episodes per day	Mean (SD)	5.4 (2.7)	5.2 (2.7)	5.3 (2.7)
Mean urinary incontinence episodes per day	Mean (SD)	6.0 (3.0)	5.8 (3.0)	5.9 (3.0)
Vaizey score	N	164	153	317
	Mean (SD)	7.6 (5.3)	6.6 (4.9)	7.1 (5.2)
	Not reported (n)	26	21	47
PISQ-12 sexually active in past 6 months	No	59 (44%)	47 (37%)	106 (41%)
	Yes	74 (56%)	79 (63%)	153 (59%)
	Not reported (n)	57	48	105
PISQ-12 score (sexually active in past 6 months)	N	73	76	149
	Mean (SD)	33.4 (7.5)	32.7 (6.7)	33.0 (7.1)
PISQ-IR total score (sexually active women)	N[1]	59	62	121
	Mean (SD)	2.9 (0.6)	3.0 (0.5)	3.0 (0.5)
PISQ-IR arousal orgasm (sexually active women)	Mean (SD)	3.3 (0.9)	3.4 (0.8)	3.4 (0.8)
PISQ-IR partner related (sexually active women)	Mean (SD)	3.4 (0.6)	3.4 (0.6)	3.4 (0.6)
PISQ-IR condition specific (sexually active women)	Mean (SD)	4.3 (0.9)	4.3 (0.7)	4.3 (0.8)
PISQ-IR global quality rating (sexually active women)	Mean (SD)	3.2 (1.2)	3.3 (1.1)	3.3 (1.2)
PISQ-IR condition impact (sexually active women)	Mean (SD)	2.9 (1.0)	2.9 (1.0)	2.9 (1.0)
PISQ-IR desire (sexually active women)	Mean (SD)	2.9 (1.0)	3.1 (0.9)	3.0 (1.0)
PISQ-IR partner related (not sexually active women)	N[a]	87	66	153
	Mean (SD)	2.2 (1.1)	2.2 (1.0)	2.2 (1.0)

Andy et al. Fecal incontinence and sexual symptoms after UUI treatment. Am J Obstet Gynecol 2019. *(continued)*

TABLE 1
Demographic and baseline characteristics for intention-to-treat population *(continued)*

Characteristic	Statistic/category	Treatment group		Total (n = 364)
		BTX (n = 190)	SNM (n = 174)	
PISQ-IR condition specific (not sexually active women)	Mean (SD)	2.9 (1.0)	3.0 (1.0)	3.0 (1.0)
PISQ-IR global quality rating (not sexually active women)	Mean (SD)	2.6 (1.3)	2.8 (1.3)	2.7 (1.3)
PISQ-IR condition impact (not sexually active women)	Mean (SD)	2.9 (1.1)	3.0 (1.2)	2.9 (1.2)

BMI, body mass index; *BTX*, onabotulinumtoxinA; *PISQ-IR*, Pelvic Organ Prolapse/Incontinence Sexual Questionnaire, IUGA-Revised; *PISQ-12*, Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire-12; *SNM*, sacral neuromodulation.

[a] Sample sizes vary slightly across subscales of the PISQ-IR owing to sporadic missed items.

Andy et al. Fecal incontinence and sexual symptoms after UUI treatment. Am J Obstet Gynecol 2019.

of the PISQ-IR subscores in both sexually active and non–sexually active women. In sexually active women, both groups demonstrated an improvement from baseline in the PISQ-IR Condition Specific Score and Condition Impact Score at 6, 12, and 24 months, with mean improvement ranging from 0.2 to 0.5 points. In non–sexually active women, there was improvement from baseline in the PISQ-IR Condition Specific Score and Global Quality Rating Score in the BTX group only and in the PISQ-IR Condition Impact Score in both the BTX and SNM groups, also with mean improvement ranging from 0.2 to 0.5 points. These improvements in subscores all correspond to "small" improvement in effect size.

Comments

In women with refractory UUI treated with SNM or BTX, we found small improvements from baseline in FI and

TABLE 2
Adjusted mean (95% confidence interval) fecal incontinence and sexual symptoms changes from baseline to 6, 12, and 24 months for the intention-to-treat population

Outcome N, adjusted mean (95% CI)	Treatment group				Difference	
	BTX (n = 190)	*P* value[a]	SNM (n = 174)	*P* value[a]	SNM - BTX	*P* value[b]
Vaizey score change from baseline	151		138			
Month 6	-1.9 (-2.6, -1.2)	<.001	-0.9 (-1.7, -0.2)	.017	1.0 (-0.1, 2.0)	.069
Month 12	-1.4 (-2.1, -0.7)	<.001	-1.1 (-1.8, -0.3)	.005	0.4 (-0.6, 1.3)	.48
Month 24	-1.4 (-2.1, -0.7)	<.001	-0.6 (-1.3, 0.1)	.11	0.8 (-0.2, 1.8)	.12
PISQ-12 score change from baseline	59		66			
Month 6	2.2 (0.7, 3.7)	.005	2.2 (0.7, 3.7)	.004	0.0 (-1.8, 1.9)	.99
Month 12	1.6 (0.0, 3.1)	.044	1.5 (-0.0, 3.0)	.054	-0.1 (-1.9, 1.8)	.95
Month 24	1.6 (0.0, 3.2)	.044	1.3 (-0.3, 2.8)	.11	-0.4 (-2.3, 1.5)	.69
PISQ-IR (sexually active women) overall score change from baseline	46		54			
Month 6	0.0 (-0.1, 0.2)	.47	0.2 (0.0, 0.3)	.010	0.1 (-0.0, 0.3)	.16
Month 12	0.1 (-0.0, 0.2)	.18	0.1 (-0.1, 0.2)	.34	-0.0 (-0.2, 0.1)	.72
Month 24	0.1 (-0.1, 0.2)	.24	0.1 (-0.0, 0.2)	.065	0.0 (-0.1, 0.2)	.65
PISQ-IR (sexually active women) arousal, orgasm score change from baseline	46		55			
Month 6	0.1 (-0.1, 0.3)	.44	0.1 (-0.1, 0.3)	.19	0.0 (-0.2, 0.3)	.73
Month 12	0.1 (-0.1, 0.3)	.35	0.1 (-0.1, 0.4)	.16	0.0 (-0.2, 0.3)	.76
Month 24	0.2 (-0.0, 0.4)	.13	0.2 (-0.0, 0.4)	.069	0.0 (-0.3, 0.3)	.91

Andy et al. Fecal incontinence and sexual symptoms after UUI treatment. Am J Obstet Gynecol 2019. *(continued)*

TABLE 2
Adjusted mean (95% confidence interval) fecal incontinence and sexual symptoms changes from baseline to 6, 12, and 24 months for the intention-to-treat population *(continued)*

	Treatment group				Difference	
Outcome N, adjusted mean (95% CI)	BTX (n = 190)	*P* value[a]	SNM (n = 174)	*P* value[a]	SNM - BTX	*P* value[b]
PISQ-IR (sexually active women) partner related score change from baseline	43		51			
Month 6	-0.0 (-0.2, 0.2)	.66	0.0 (-0.1, 0.2)	.71	0.1 (-0.1, 0.3)	.50
Month 12	-0.0 (-0.2, 0.2)	.78	-0.0 (-0.2, 0.2)	.96	0.0 (-0.2, 0.2)	.84
Month 24	-0.1 (-0.3, 0.1)	.40	0.0 (-0.2, 0.2)	.99	0.1 (-0.1, 0.3)	.45
PISQ-IR (sexually active women) condition specific score change from baseline	46		55			
Month 6	0.4 (0.2, 0.6)	<.001	0.2 (0.0, 0.4)	.039	-0.2 (-0.4, 0.1)	.13
Month 12	0.3 (0.1, 0.5)	.007	0.3 (0.1, 0.5)	.002	0.0 (-0.2, 0.3)	.87
Month 24	0.4 (0.2, 0.6)	<.001	0.3 (0.1, 0.5)	.002	-0.1 (-0.3, 0.2)	.50
PISQ-IR (sexually active women) global quality rating score change from baseline	45		54			
Month 6	0.1 (-0.3, 0.4)	.75	0.3 (-0.0, 0.6)	.10	0.2 (-0.2, 0.6)	.32
Month 12	0.1 (-0.2, 0.5)	.48	-0.0 (-0.4, 0.3)	.80	-0.2 (-0.6, 0.2)	.43
Month 24	0.3 (-0.1, 0.6)	.10	0.2 (-0.1, 0.5)	.24	-0.1 (-0.5, 0.3)	.63
PISQ-IR (sexually active women) condition impact score change from baseline	46		54			
Month 6	0.4 (0.2, 0.7)	<.001	0.5 (0.2, 0.7)	<.001	0.0 (-0.3, 0.3)	.92
Month 12	0.3 (0.1, 0.5)	.018	0.4 (0.2, 0.6)	<.001	0.1 (-0.2, 0.4)	.50
Month 24	0.3 (0.0, 0.5)	.021	0.4 (0.2, 0.6)	<.001	0.1 (-0.2, 0.4)	.41
PISQ-IR (sexually active women) desire score change from baseline	46		53			
Month 6	-0.0 (-0.2, 0.2)	.84	0.0 (-0.2, 0.2)	.94	0.0 (-0.2, 0.3)	.82
Month 12	0.1 (-0.1, 0.4)	.22	-0.0 (-0.2, 0.2)	.77	-0.2 (-0.4, 0.1)	.22
Month 24	-0.1 (-0.3, 0.1)	.48	-0.0 (-0.2, 0.2)	.68	0.0 (-0.2, 0.3)	.78
PISQ-IR (not sexually active women) partner related score change from baseline	75		57			
Month 6	-0.1 (-0.3, 0.1)	.48	-0.2 (-0.4, 0.1)	.18	-0.1 (-0.4, 0.2)	.58
Month 12	-0.1 (-0.3, 0.1)	.48	-0.3 (-0.5, -0.0)	.028	-0.2 (-0.5, 0.1)	.22
Month 24	-0.1 (-0.3, 0.1)	.48	-0.2 (-0.5, 0.0)	.065	-0.2 (-0.5, 0.2)	.34
PISQ-IR (not sexually active women) condition specific score change from baseline	71		56			
Month 6	0.3 (0.1, 0.5)	.005	0.2 (-0.0, 0.5)	.058	-0.1 (-0.4, 0.2)	.63
Month 12	0.2 (0.0, 0.4)	.025	0.2 (-0.1, 0.4)	.18	-0.1 (-0.4, 0.2)	.65
Month 24	0.3 (0.1, 0.5)	.003	0.1 (-0.1, 0.4)	.26	-0.2 (-0.5, 0.1)	.24
PISQ-IR (not sexually active women) global quality rating score change from baseline	70		57			
Month 6	0.4 (0.1, 0.6)	.003	0.3 (0.1, 0.6)	.018	-0.0 (-0.4, 0.3)	.80
Month 12	0.4 (0.2, 0.6)	<.001	0.2 (-0.1, 0.5)	.13	-0.2 (-0.6, 0.1)	.17
Month 24	0.5 (0.2, 0.7)	<.001	0.2 (-0.0, 0.5)	.075	-0.2 (-0.6, 0.1)	.17

Andy et al. Fecal incontinence and sexual symptoms after UUI treatment. Am J Obstet Gynecol 2019. *(continued)*

TABLE 2
Adjusted mean (95% confidence interval) fecal incontinence and sexual symptoms changes from baseline to 6, 12, and 24 months for the intention-to-treat population *(continued)*

Outcome N, adjusted mean (95% CI)	Treatment group				Difference	
	BTX (n = 190)	*P* value[a]	SNM (n = 174)	*P* value[a]	SNM - BTX	*P* value[b]
PISQ-IR (not sexually active women) condition impact score change from baseline	71		58			
Month 6	0.4 (0.1, 0.6)	.001	0.5 (0.3, 0.7)	<.001	0.1 (-0.2, 0.4)	.41
Month 12	0.5 (0.3, 0.7)	<.001	0.4 (0.2, 0.6)	<.001	-0.0 (-0.3, 0.3)	.77
Month 24	0.5 (0.3, 0.7)	<.001	0.4 (0.2, 0.6)	<.001	-0.1 (-0.4, 0.2)	.56

Adjusted means and 95% CI are from a mixed linear repeated measures model with month as a categorical effect and adjustment for site, age group strata, and baseline value. N is the number of participants with baseline and at least 1 postbaseline score.

CI, confidence interval; other abbreviations as in Table 1.

[a] *P* value from within-group test of adjusted mean change from baseline = 0; [b] *P* value from treatment group comparison of adjusted mean change from baseline.

Andy et al. Fecal incontinence and sexual symptoms after UUI treatment. Am J Obstet Gynecol 2019.

sexual symptom scores, which were similar in both groups; however, although statistically significant, the improvements did not uniformly meet a clinically meaningful difference. Only in the subgroup of women with clinically significant FI symptoms at baseline was the symptom improvement in bowel symptoms clinically meaningful. Furthermore, this improvement was similar following treatment with SNM compared with BTX. These findings may help clinicians when counseling women considering treatment for refractory UUI.

In our study, FI symptoms improved following treatment for refractory UUI for women with clinically significant symptoms at baseline. This finding is consistent with others that have reported improvement in FI symptoms following SNM for UUI, although the retrospective nature of those studies and lack of use of validated questionnaires make it challenging to directly compare the results.[17,18] In a small retrospective cohort of women with symptomatic UUI and FI at baseline, Kim et al[19] reported statistically significant and clinically meaningful improvement in Cleveland Clinic Fecal Incontinence Score with median follow-up of 14 months following SNM placement; however,

TABLE 3
Adjusted mean (95% confidence interval) Vaizey score change from baseline to 6, 12, and 24 months by baseline Vaizey score for the intention-to-treat population

Outcome N, adjusted mean (95% CI)	Treatment group				Difference	
	BTX (n = 190)	*P* value[a]	SNM (n = 174)	*P* value[a]	SNM - BTX	*P* value[b]
Baseline Vaizey score ≥12						
Vaizey score change from baseline	33		22			
Month 6	-5.1 (-7.3, -2.8)	<.001	-5.6 (-8.5, -2.6)	<.001	-0.5 (-4.2, 3.2)	.78
Month 12	-4.5 (-6.6, -2.4)	<.001	-4.5 (-7.4, -1.7)	.002	0.0 (-3.4, 3.5)	.99
Month 24	-5.8 (-8.0, -3.7)	<.001	-3.9 (-6.9, -1.0)	.009	1.9 (-1.7, 5.5)	.29
Baseline Vaizey score <12						
Vaizey score change from baseline	118		116			
Month 6	-1.0 (-1.8, -0.3)	.007	0.2 (-0.5, 1.0)	.51	1.3 (0.3, 2.3)	.013
Month 12	-0.6 (-1.3, 0.1)	.11	-0.1 (-0.8, 0.7)	.86	0.5 (-0.5, 1.5)	.29
Month 24	-0.1 (-0.9, 0.6)	.71	0.4 (-0.3, 1.1)	.27	0.5 (-0.4, 1.5)	.28

Adjusted means and 95% CI are from a mixed linear repeated measures model for each subgroup with month as a categorical effect and with adjustment for site, age group, and baseline value. N is the number of participants with baseline and at least one post-baseline score.

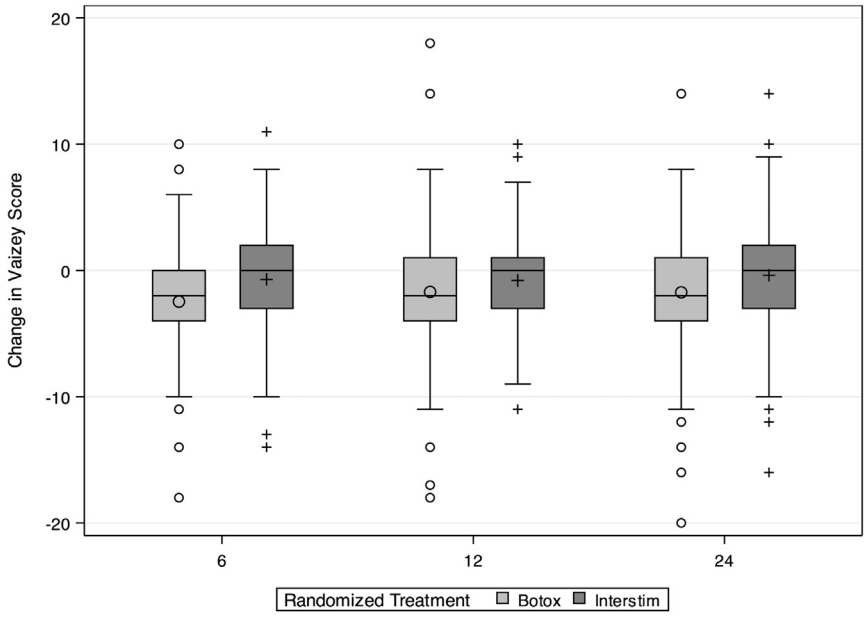
P values for interaction of baseline Vaizey score and each time point when added to the main model: 6 months 0.42; 12 months 0.64; 24 months 0.62.

BTX, onabotulinumtoxinA; *CI*, confidence interval; *SNM*, sacral neuromodulation.

[a] *P* value for within-group test of adjusted mean change from baseline = 0; [b] *P* value for treatment group comparison of adjusted mean change from baseline.

Andy et al. Fecal incontinence and sexual symptoms after UUI treatment. Am J Obstet Gynecol 2019.

FIGURE
Change in Vaizey score from baseline in intent-to-treat population



Andy et al. Fecal incontinence and sexual symptoms after UUI treatment. Am J Obstet Gynecol 2019.

baseline FI was poorly defined and characterized. Importantly, we identified that in women with refractory UUI, a clinically meaningful improvement in bowel symptoms can be expected in women with Vaizey score ≥12 at baseline.

Our study design allowed for direct comparison between SNM and BTX; surprisingly, we found that improvement in FI symptoms were similar following treatment with BTX compared to SNM. SNM is a U.S. Food and Drug Administration–approved treatment for FI and is believed to result in neuromodulation of bowel activity via stimulation of the pudendal afferent somatic fibers.[20] Thus, we had expected that it would have a more substantial impact on FI symptoms compared to BTX. The lack of difference in improvement in FI symptoms between SNM and BTX may indicate that rather than specific impact on bowel mechanisms, the improvement in FI symptoms seen with SNM and BTX treatment reflects the impact of UUI treatment on improvement in global quality of life, including perception of bowel symptoms. Alternatively, our findings may provide clinical evidence of pelvic organ cross-sensitization, a phenomenon in which disease, and by extension therapeutic intervention, in 1 pelvic organ impacts another pelvic organ. Neural "cross-talk" in the pelvis exists under normal conditions and is necessary for the normal regulation of sexual, bladder, and bowel function.[21] Animal studies have demonstrated an association between dysfunction in the lower urinary tract and the gastrointestinal tract such that, for example, acute cystitis may result in lower colorectal sensory thresholds and an acute colitis may result in irritative voiding symptoms.[22] Thus, intradetrusor BTX could have an impact on bowel function by a mechanism of pelvic organ cross-sensitization resulting in similar effects on FI symptoms as SNM. Further mechanistic research is required to confirm cross-sensitization and future therapies may be designed to target the "key organ," that is, the one that confers the most global benefit. Nonetheless, our findings may reassure women undergoing treatment for refractory UUI, especially in those with significant FI at baseline, that they can expect improvements in their symptoms if they elect to pursue treatment with BTX instead of SNM.

We found that sexually active women had statistically significant improvements in sexual function following SNM and BTX, although these only represented "small" improvement in effect size from baseline on the PISQ-12 questionnaire. Parnell et al,[23] in a cohort of women treated with SNM for UUI, found significant improvement of "moderate" effect size in sexual symptom scores also using the PISQ-12 instrument. Following BTX for UUI, Balzarro et al[4] also reported statistically significant improvement in overall sexual function, although these authors used a different instrument to measure sexual function. Taken together with our findings, this suggests that in sexually active women undergoing treatment for refractory UUI, at least small improvements in sexual function can be expected, with similar improvement with either SNM or BTX.

Sexual dysfunction in women is complex and can be related to general issues unrelated to the pelvic floor, such as desire, arousal, and the ability to obtain an orgasm. The mechanism by which treatment for UUI with SNM or BTX may improve sexual function is uncertain. In our study, we found small improvements from baseline in the Condition Specific and Condition Impact subscales—but not in the other subscales such as Arousal/Orgasm, Partner Related, and Desire—of the PISQ-IR questionnaire in sexually active women. This suggests that the improvement in sexual function was a result of improvement in urinary symptoms and not other aspects of sexual function. Using a different instrument to examine domains of sexual function, Parnell et al[23] reported significant improvements following SNM in the desire domain of sexual function but not the arousal, orgasm, or lubrication domains. In contrast, Balzarro et al[4] reported significant improvements in arousal, lubrication, orgasm, and satisfaction domains after BTX injection. Given these conflicting results, the impact of treatments for refractory UUI on sexual function beyond their

effect on improving urinary symptoms requires further investigation. Nevertheless, the positive impact of SNM and BTX on both urinary symptoms and sexual function further underscores the importance of providing effective treatments for women with refractory UUI.

The strengths of our study include the use of condition-specific validated measures of sexual function and FI, prospective data collected by research staff masked to the subjects' randomized group assignment, and the geographical diversity of the participating study sites. There is limited evidence in terms of the effect of neuromodulation, especially BTX, on bowel and sexual function; therefore, our paper substantially adds to the literature to help guide clinicians. Study limitations include mild baseline FI symptoms in our study population, which inherently limits the degree of improvement possible and generalizability of our findings to women with concurrent severe FI. We sought to mitigate this issue by performing a subanalysis of women with more significant baseline FI symptoms (ie, higher Vaizey scores) and noted similarly that there was no difference in improvement in symptoms between the 2 interventions. Importantly, the improvement seen in this group did meet the clinically meaningful difference, highlighting the likely positive impact of these treatments on FI symptoms. Nonetheless, it is important to note that the subgroup of women with Vaizey score $\geq$12 only included 14% of the study population. Second, a quarter of our study population did not complete the sexual symptom questionnaires at baseline and fewer than 60% of our population were sexually active at baseline; thus, the data need to be interpreted cautiously. The importance of the small improvements we noted in sexual function would be better explored in a larger trial with a more affected target population. Finally, given the complex nature of female sexual function, although we used well-validated instruments to assess change in sexual function, there are likely other social and emotional aspects of sexual function that our study could not assess.

Our results suggest that women with refractory UUI treated with either SNM or BTX can expect some improvement in bowel and sexual function, with no difference between the 2 interventions. Women with significant FI symptoms at baseline will have clinically meaningful improvement, with no difference between the treatments. ■

Acknowledgments

We thank the coordinators and all those who made this work possible, including the following: Coordinators: University of Alabama: Velria B. Willis, RN, BSN, CCRC, Nancy B. Saxon, RN, BSN, Kathy S. Carter, RN, BSN; Brown University: Alexandra Lynch, Allegra Parrillo; University of California, San Diego/Kaiser San Diego/Kaiser Downey: JoAnn Columbo, Gisselle Zazueta-Damian, Linda M. Mackinnon, MPH; Cleveland Clinic: Andrea Aaby, BS, Ly Pung, RN; Duke University: Akira Hayes, MS, 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: University of Alabama: R. Edward Varner, MD, Tracey S. Wilson, MD, L. Keith Lloyd, MD, Holly Richter, MD, PhD, Robert L. Holley, MD, Alicia C. Ballard, MD, David R. Ellington, MD, Patricia S Goode, MD; Brown University: Vivian W. Sung, MD, MPH, Charles R. Rardin, MD, B. Star Hampton, MD, Vivian Sung, MD, Kyle J. Wohlrab, MD, Cassandra L. Carberry, MD, MS; University of California, San Diego/Kaiser San Diego/Kaiser Downey: Emily Lukacz, MD, Charles Nager, MD, Shawn A. Menefee, MD, Jasmine Tan-Kim, MD, Karl M. Luber, MD, Gouri B. Diwadkar, MD, Michael Albo, MD, John N. Nguyen, MD, Sharon Jakus-Walman, MD; Cleveland Clinic: Bradley Gill, MD, Matthew Barber, MD, MHS, Marie F. R. Paraiso, MD, Mark Walters, MD, Cecile Unger, MD, MPH, Beri Ridgeway, MD; Duke University: Amie Kawasaki, MD, Nazema Y. Siddiqui, MD, Anthony G. Visco, MD, Alison C. Weidner, MD; Oregon Health Sciences University: S. Renee Edwards, MD, Mary Anna Denman, MD, Kamran Sajadi, MD; University of New Mexico: Rebecca Rogers, MD, Yuko Komesu, MD, Peter Jeppson, MD, Sara Cichowski, MD; University of Pennsylvania: Lily A. Arya, MD, Ariana L. Smith, MD, Heidi Harvie, MD; University of Pittsburgh: Michael Bonidie, MD, Christopher Chermansky, MD, Pamela Moalli, PhD, MD, Jonathan Shepherd, MD, Gary Sutkin, MD, Halina Zyczynski, MD; RTI International: Marie Gantz, PhD.

References

1. Nygaard I, Barber MD, Burgio KL, et al; Pelvic Floor Disorders Network. Prevalence of symptomatic pelvic floor disorders in US women. JAMA 2008;300(11):1311–6.
2. Cameron AP, Smith AR, Lai HH, et al; LURN Study Group. Bowel function, sexual function, and symptoms of pelvic organ prolapse in women with and without urinary incontinence. Neurourol Urodyn 2018;37(8):2586–96.
3. Jadav AM, Wadhawan H, Jones GL, Wheldon LW, Radley SC, Brown SR. Does sacral nerve stimulation improve global pelvic function in women? Colorectal Dis 2013;15(7):848–57.
4. Balzarro M, Rubilotta E, Braga A, et al. OnabotulinumtoxinA detrusor injection improves female sexual function in women with overactive bladder wet syndrome. Eur J Obstet Gynecol Reprod Biol 2018;225:228–31.
5. Amundsen CL, Richter HE, Menefee S, et al. The refractory overactive bladder: sacral neuromodulation vs botulinum toxin assessment: ROSETTA trial. Contemp Clin Trials 2014;37(2):272–83.
6. Vaizey CJ, Carapeti E, Cahill JA, Kamm MA. Prospective comparison of faecal incontinence grading systems. Gut 1999;44:77–80.
7. Bols EM, Hendriks EJ, Deutekom M, et al. Inconclusive psychometric properties of the Vaizey score in fecally incontinent patients: A prospective cohort study. Neurourol Urodyn 2010;29:370–7.
8. Landefeld CS, Bowers BJ, Feld AD, et al. National institutes of health state-of-the-science conference statement: Prevention of fecal and urinary incontinence in adults. Ann Intern Med 2008;148(6):449–58.
9. Norton C, Cody JD, Hosker G. Biofeedback and/or sphincter exercises for the treatment of faecal incontinence in adults. Cochrane Database Syst Rev 2007;4.
10. Deutekom M, Terra MP, Dobben AC, et al. Selecting an outcome measure for evaluating treatment in fecal incontinence. Dis Colon Rectum 2005;48:2294–301.
11. Jelovsek ER, Markland AD, Whitehead WE, et al. Controlling anal incontinence in women by performing anal exercises with biofeedback or loperamide (CAPABLe) trial: Design and methods. Contemp Clin Trials 2015;44:164–74.
12. Rogers RG, Coates KW, Kammerer-Doak D, Khalsa S, Qualls C. A short form of the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12) Int Urogynecol J Pelvic Floor Dysfunct 2003;14:164–8; erratum in: Int Urogynecol J Pelvic Floor Dysfunct 2004;15: 219.
13. Rogers RG, Rockwood TH, Constantine ML, et al. A new measure of sexual function in women with pelvic floor disorders (PFD): the Pelvic Organ Prolapse/Incontinence Sexual Questionnaire, IUGA-Revised (PISQ-IR). Int Urogynecol J 2013;24(7):1091–103.
14. Crosby RD, Kolotkin RL, Williams GR. Defining clinically meaningful change in health-related quality of life. J Clin Epidemiol 2003;56(5):395–407.
15. Amundsen CL, Richter HE, Menefee SA, et al. OnabotulinumtoxinA vs sacral

neuromodulation on refractory urgency urinary incontinence in women: a randomized clinical trial. JAMA 2016;316(13):1366–74.
16. Amundsen CL, Komesu YM, Chermansky C, et al. Two-year outcomes of sacral neuromodulation versus onabotulinumtoxina for refractory urgency urinary incontinence: a randomized trial. Eur Urol 2018;74(1):66–73.
17. Leong RK, Marcelissen TA, Nieman FH, et al. Satisfaction and patient experience with sacral neuromodulation: results of a single center sample survey. J Urol 2011;185:588–92.
18. Caremel R, Damon H, Ruffion A, et al. Can sacral neuromodulation improve minor incontinence symptoms in doubly incontinent patients successfully treated for major incontinence symptoms? Urology 2012;79(1):80–5.
19. Kim DH, Faruqui N, Ghoniem GM. Sacral neuromodulation outcomes in patients with urge urinary incontinence and concomitant urge fecal incontinence. Female Pelvic Med Reconstr Surg 2010;16:171–8.
20. Gourcerol G, Vitton V, Leroi AM, Michot F, Abysique A, Bouvier M. How sacral nerve stimulation works in patients with faecal incontinence. Colorectal Dis 2011;13(8):e203–11.
21. Ustinova EE, Fraser MO, Pezzone MA. Cross-talk and sensitization of bladder afferent nerves. Neurourol Urodyn 2010;29(1):77–81.
22. Pezzone MA, Liang R, Fraser MO. A model of neural cross-talk and irritation in the pelvis: implications for the overlap of chronic pelvic pain disorders. Gastroenterology 2005;128(7):1953–64.
23. Parnell BA, Howard JF, Geller EJ. The effect of sacral neuromodulation on pudendal nerve function and female sexual function. Neurourol Urodyn 2015;34:456–60.

Author and article information

Department of Obstetrics and Gynecology, University of Pennsylvania, Philadelphia, Pennsylvania (Dr Andy); Department of Obstetrics and Gynecology, Duke University Medical Center, Durham, North Carolina (Dr Amundsen); Department of Medicine, University of Alabama at Birmingham, Birmingham, Alabama (Dr Markland); Departments of Obstetrics and Gynecology and Surgery, University of New Mexico Health Sciences Center, Albuquerque, New Mexico (Dr Dunivan); Department of Obstetrics and Gynecology Kaiser Permanente, San Diego, California (Dr Dyer); Department of Obstetrics and Gynecology, Alpert Medical School of Brown University, Providence, Rhode Island (Dr Korbly); Department of Obstetrics, Gynecology and Reproductive Sciences, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania (Dr Bradley); Department of Urology, Cleveland Clinic. Cleveland, Ohio (Dr Vasavada); The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland (Ms Mazloomdoost); and RTI International, Research Triangle Park, North Carolina (Ms Honeycutt and Dr Thomas).

Received Dec. 31, 2018; revised May 17, 2019; accepted June 10, 2019.

Supported by grants from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development and the National Institutes of Health Office of Research on Women's Health.

The authors report the following potential conflicts of interest: Uduak U. Andy: PI Grant R03-AG-053277-01, National Institute on Aging, NIH; PI Industry Grant, Pelvalon Inc; Gena Dunivan and Keisha Y. Dyer: PI Industry Grant, Pelvalon Inc; Sandip Vasavada: Consulting, Medtronic, Allergan, BlueWind, and Amphora. The following authors report no conflicts of interest: Cindy L. Amundsen, Emily Honeycutt, Alayne D. Markland, Nicole B. Korbly, Megan Bradley, Donna Mazloomdoost, and Sonia Thomas.

ClinicalTrials.gov Identifier: NCT01502956.

Corresponding author: Uduak Andy, MD. uduakumoh.andy@uphs.upenn.edu

Appendix
Clinical responder results

TABLE S1
Demographic and baseline characteristics for clinical responder population

Characteristic	Statistic/category	Treatment group		
		BTX (n = 159)	SNM (n = 139)	Total (n = 298)
Race	White	131 (2%)	117 (84%)	248 (83%)
	Black/African American	19 (2%)	16 (12%)	35 (12%)
	American Indian/Alaskan Native	2 (1%)	1 (1%)	3 (1%)
	Asian	1 (1%)	1 (1%)	2 (1%)
	Other	5 (3%)	3 (2%)	8 (3%)
	Unknown/not reported	1 (1%)	1 (1%)	2 (1%)
Ethnicity	Hispanic/Latina	15 (9%)	8 (6%)	23 (8%)
	Not Hispanic/Latina	140 (88%)	128 (92%)	268 (90%)
	Unknown/not reported	4 (3%)	3 (2%)	7 (2%)
Age at baseline (years)	Mean (SD)	62.4 (11.0)	62.7 (11.8)	62.5 (11.4)
BMI (kg/m^2)	Mean (SD)	32.4 (8.9)	32.4 (7.8)	32.4 (8.3)
Functional comorbidity index	Mean (SD)	3.7 (2.2)	3.6 (2.3)	3.6 (2.2)
Current smoker	No	142 (89%)	124 (89%)	266 (89%)
	Yes	17 (11%)	15 (11%)	32 (11%)
Menopausal status	Postmenopausal	137 (86%)	117 (84%)	254 (85%)
	Premenopausal	16 (10%)	16 (12%)	32 (11%)
	Not sure	6 (4%)	6 (4%)	12 (4%)
Mean urge urinary incontinence episodes per day	Mean (SD)	5.3 (2.6)	5.0 (2.1)	5.2 (2.4)
Mean urinary incontinence episodes per day	Mean (SD)	5.9 (2.9)	5.6 (2.3)	5.7 (2.7)
Vaizey score	N	138	122	260
	Mean (SD)	7.2 (5.2)	6.4 (4.7)	6.8 (5.0)
	Not reported (N)	21	17	38
PISQ-12 sexually active in past 6 months	No	46 (42%)	40 (39%)	86 (41%)
	Yes	63 (58%)	62 (61%)	125 (59%)
	Not reported (N)	50	37	87
PISQ-12 score (sexually active in past 6 months)	N	63	60	123
	Mean (SD)	33.7 (7.7)	32.4 (7.0)	33.1 (7.4)
PISQ-IR total score (sexually active women)	N[a]	49	48	97
	Mean (SD)	2.9 (0.6)	3.0 (0.5)	3.0 (0.5)
PISQ-IR arousal orgasm (sexually active women)	Mean (SD)	3.3 (0.9)	3.5 (0.8)	3.4 (0.8)
PISQ-IR partner related (sexually active women)	Mean (SD)	3.4 (0.6)	3.3 (0.6)	3.3 (0.6)
PISQ-IR condition specific (sexually active women)	Mean (SD)	4.3 (0.9)	4.4 (0.7)	4.4 (0.8)
PISQ-IR global quality rating (sexually active women)	Mean (SD)	3.3 (1.1)	3.4 (1.1)	3.3 (1.1)
PISQ-IR condition impact (sexually active women)	Mean (SD)	2.9 (1.0)	2.9 (1.0)	2.9 (1.0)
PISQ-IR desire (sexually active women)	Mean (SD)	2.8 (1.0)	3.2 (0.9)	3.0 (1.0)

Andy et al. Fecal incontinence and sexual symptoms after UUI treatment. Am J Obstet Gynecol 2019. *(continued)*

TABLE S1
Demographic and baseline characteristics for clinical responder population *(continued)*

Characteristic	Statistic/category	Treatment group		
		BTX (n = 159)	SNM (n = 139)	Total (n = 298)
PISQ-IR partner related (not sexually active women)	N[a]	75	54	129
	Mean (SD)	2.3 (1.0)	2.2 (1.0)	2.2 (1.0)
PISQ-IR condition specific (not sexually active women)	Mean (SD)	2.9 (1.0)	3.0 (1.0)	3.0 (1.0)
PISQ-IR global quality rating (not sexually active women)	Mean (SD)	2.6 (1.3)	2.7 (1.3)	2.6 (1.3)
PISQ-IR condition impact (not sexually active women)	Mean (SD)	2.9 (1.1)	3.0 (1.2)	2.9 (1.1)

BMI, body mass index; *BTX*, onabotulinumtoxinA; *PISQ-IR*, Pelvic Organ Prolapse/Incontinence Sexual Questionnaire, IUGA-Revised; *PISQ-12*, Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire-12; *SNM*, sacral neuromodulation.

[a] Sample sizes vary slightly across subscales of the PISQ-IR owing to sporadic missed items.

Andy et al. Fecal incontinence and sexual symptoms after UUI treatment. Am J Obstet Gynecol 2019.

TABLE S2
Adjusted mean (95% confidence interval) fecal incontinence and sexual symptoms changes from baseline to 6, 12, and 24 months for the clinical responder population

	Treatment group				Difference	
Outcome N, adjusted mean (95% CI)	BTX (n = 159)	*P* value[a]	SNM (n = 139)	*P* value[a]	SNM - BTX	*P* value[b]
Vaizey score change from baseline	127		114			
Month 6	-2.1 (-2.9, -1.3)	<.001	-1.0 (-1.9, -0.1)	.025	1.1 (-0.1, 2.2)	.062
Month 12	-1.5 (-2.2, -0.7)	<.001	-0.8 (-1.7, 0.0)	.054	0.6 (-0.4, 1.7)	.24
Month 24	-1.2 (-2.0, -0.4)	.003	-0.3 (-1.1, 0.5)	.50	0.9 (-0.2, 2.0)	.11
PISQ-12 score change from baseline	54		54			
Month 6	3.1 (1.5, 4.7)	<.001	3.4 (1.7, 5.1)	<.001	0.3 (-1.6, 2.1)	.78
Month 12	2.5 (0.9, 4.0)	.002	2.6 (0.8, 4.4)	.004	0.2 (-1.7, 2.0)	.87
Month 24	2.2 (0.6, 3.8)	.008	2.8 (1.1, 4.5)	.002	0.6 (-1.3, 2.4)	.56
PISQ-IR (sexually active women) overall score change from baseline	42		44			
Month 6	0.1 (-0.0, 0.3)	.070	0.2 (0.1, 0.4)	<.001	0.1 (-0.0, 0.3)	.15
Month 12	0.2 (0.0, 0.3)	.011	0.2 (0.0, 0.3)	.019	-0.0 (-0.2, 0.2)	.97
Month 24	0.1 (-0.0, 0.3)	.051	0.2 (0.1, 0.3)	.001	0.1 (-0.1, 0.2)	.29
PISQ-IR (sexually active women) arousal, orgasm score change from baseline	42		45			
Month 6	0.1 (-0.1, 0.3)	.38	0.1 (-0.1, 0.4)	.24	0.0 (-0.2, 0.3)	.83
Month 12	0.1 (-0.1, 0.4)	.25	0.2 (-0.1, 0.4)	.19	0.0 (-0.3, 0.3)	.89
Month 24	0.2 (-0.1, 0.4)	.13	0.2 (0.0, 0.4)	.049	0.0 (-0.2, 0.3)	.75
PISQ-IR (sexually active women) partner related score change from baseline	41		41			
Month 6	0.0 (-0.2, 0.2)	.82	0.1 (-0.1, 0.3)	.17	0.1 (-0.1, 0.4)	.35
Month 12	0.0 (-0.1, 0.2)	.69	0.1 (-0.1, 0.3)	.27	0.1 (-0.2, 0.3)	.54
Month 24	-0.0 (-0.2, 0.2)	.93	0.1 (-0.1, 0.3)	.26	0.1 (-0.1, 0.4)	.33
PISQ-IR (sexually active women) condition specific score change from baseline	42		45			
Month 6	0.4 (0.2, 0.6)	<.001	0.4 (0.2, 0.6)	<.001	-0.1 (-0.3, 0.2)	.53
Month 12	0.3 (0.2, 0.5)	<.001	0.4 (0.2, 0.6)	<.001	0.1 (-0.1, 0.3)	.45
Month 24	0.4 (0.2, 0.6)	<.001	0.4 (0.3, 0.6)	<.001	0.0 (-0.2, 0.3)	.75
PISQ-IR (sexually active women) global quality rating score change from baseline	42		44			
Month 6	0.2 (-0.1, 0.6)	.24	0.5 (0.1, 0.8)	.008	0.3 (-0.2, 0.7)	.24
Month 12	0.3 (-0.0, 0.6)	.068	0.2 (-0.2, 0.5)	.31	-0.1 (-0.6, 0.3)	.56
Month 24	0.4 (0.1, 0.7)	.022	0.4 (0.1, 0.7)	.018	0.0 (-0.4, 0.4)	.97
PISQ-IR (sexually active women) condition impact score change from baseline	42		44			
Month 6	0.5 (0.3, 0.7)	<.001	0.6 (0.4, 0.8)	<.001	0.1 (-0.2, 0.4)	.54
Month 12	0.4 (0.2, 0.6)	<.001	0.5 (0.3, 0.8)	<.001	0.2 (-0.1, 0.5)	.21
Month 24	0.3 (0.1, 0.6)	.003	0.5 (0.3, 0.7)	<.001	0.2 (-0.1, 0.5)	.19

Andy et al. Fecal incontinence and sexual symptoms after UUI treatment. Am J Obstet Gynecol 2019.

(continued)

TABLE S2
Adjusted mean (95% confidence interval) fecal incontinence and sexual symptoms changes from baseline to 6, 12, and 24 months for the clinical responder population *(continued)*

Outcome N, adjusted mean (95% CI)	Treatment group				Difference	
	BTX (n = 159)	*P* value[a]	SNM (n = 139)	*P* value[a]	SNM - BTX	*P* value[b]
PISQ-IR (sexually active women) desire score change from baseline	42		43			
Month 6	0.1 (-0.2, 0.3)	.64	0.0 (-0.2, 0.3)	.77	-0.0 (-0.3, 0.3)	.89
Month 12	0.2 (-0.0, 0.4)	.12	0.0 (-0.2, 0.3)	.82	-0.1 (-0.4, 0.1)	.30
Month 24	-0.1 (-0.3, 0.2)	.55	0.0 (-0.2, 0.2)	.87	0.1 (-0.2, 0.4)	.53
PISQ-IR (not sexually active women) partner related score change from baseline	63		49			
Month 6	-0.0 (-0.3, 0.2)	.75	-0.2 (-0.5, 0.1)	.16	-0.2 (-0.5, 0.2)	.38
Month 12	-0.1 (-0.3, 0.2)	.48	-0.3 (-0.6, 0.0)	.053	-0.2 (-0.6, 0.2)	.30
Month 24	-0.1 (-0.4, 0.2)	.44	-0.3 (-0.5, 0.0)	.083	-0.2 (-0.5, 0.2)	.42
PISQ-IR (not sexually active women) condition specific score change from baseline	59		49			
Month 6	0.4 (0.2, 0.7)	<.001	0.2 (-0.0, 0.5)	.064	-0.2 (-0.5, 0.2)	.28
Month 12	0.2 (0.0, 0.4)	.033	0.2 (-0.0, 0.5)	.090	-0.0 (-0.3, 0.3)	.90
Month 24	0.4 (0.2, 0.7)	<.001	0.2 (-0.1, 0.4)	.22	-0.3 (-0.6, 0.1)	.12
PISQ-IR (not sexually active women) global quality rating score change from baseline	60		49			
Month 6	0.4 (0.2, 0.7)	<.001	0.4 (0.1, 0.6)	.011	-0.1 (-0.4, 0.3)	.74
Month 12	0.4 (0.2, 0.6)	<.001	0.3 (-0.0, 0.5)	.064	-0.2 (-0.5, 0.2)	.38
Month 24	0.5 (0.2, 0.7)	<.001	0.2 (-0.1, 0.5)	.17	-0.3 (-0.6, 0.1)	.11
PISQ-IR (not sexually active women) condition impact score change from baseline	60		49			
Month 6	0.5 (0.2, 0.7)	<.001	0.5 (0.2, 0.7)	.001	-0.0 (-0.4, 0.3)	.86
Month 12	0.5 (0.3, 0.7)	<.001	0.4 (0.1, 0.7)	.002	-0.1 (-0.4, 0.2)	.53
Month 24	0.5 (0.3, 0.8)	<.001	0.4 (0.1, 0.6)	.004	-0.2 (-0.5, 0.2)	.38

Adjusted means and 95% CI are from a mixed linear repeated measures model with month as a categorical effect and adjustment for site, age group strata, and baseline value. N is the number of participants with baseline and at least 1 postbaseline score.

CI, confidence interval; other abbreviations as in Table S1.

[a] *P* value from within-group test of adjusted mean change from baseline = 0; [b] *P* value from treatment group comparison of adjusted mean change from baseline.

Andy et al. Fecal incontinence and sexual symptoms after UUI treatment. Am J Obstet Gynecol 2019.

TABLE S3
Adjusted mean (95% confidence interval) Vaizey score change from baseline to 6, 12, and 24 months by baseline Vaizey score for the clinical responder population

	Treatment group				Difference	
Outcome N, adjusted mean (95% CI)	BTX (n = 159)	*P* value[a]	SNM (n = 139)	*P* value[a]	SNM - BTX	*P* value[b]
Baseline Vaizey score ≥12						
Vaizey score change from baseline	25		17			
Month 6	-6.2 (-8.8, -3.6)	<.001	-6.1 (-9.5, -2.7)	.001	0.1 (-4.1, 4.4)	.96
Month 12	-5.1 (-7.6, -2.5)	<.001	-4.5 (-7.7, -1.4)	.006	0.6 (-3.5, 4.6)	.78
Month 24	-5.8 (-8.3, -3.2)	<.001	-4.5 (-7.7, -1.3)	.007	1.3 (-2.8, 5.3)	.53
Baseline Vaizey score <12						
Vaizey score change from baseline	102		97			
Month 6	-1.1 (-1.9, -0.2)	.01	0.2 (-0.7, 1.0)	.72	1.2 (0.1, 2.3)	.034
Month 12	-0.5 (-1.3, 0.2)	.18	0.2 (-0.7, 1.0)	.70	0.7 (-0.4, 1.8)	.21
Month 24	-0.0 (-0.8, 0.8)	.99	0.8 (-0.1, 1.6)	.07	0.8 (-0.3, 1.9)	.17

Adjusted means and 95% CI are from a mixed linear repeated measures model for each subgroup with month as a categorical effect and with adjustment for site, age group, and baseline value. N is the number of participants with baseline and at least 1 postbaseline score.

P values for interaction of baseline Vaizey score and each time point when added to the main model: 6 months 0.67; 12 months 0.85; 24 months 0.81.

BTX, onabotulinumtoxinA; *CI*, confidence interval; *SNM*, sacral neuromodulation.

[a] *P* value for within-group test of adjusted mean change from baseline = 0; [b] *P* value for treatment group comparison of adjusted mean change from baseline.

Andy et al. Fecal incontinence and sexual symptoms after UUI treatment. Am J Obstet Gynecol 2019.