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# Midurethral Sling vs OnabotulinumtoxinA in Females With Urinary Incontinence The MUSA Randomized Clinical Trial

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**IMPORTANCE** Mixed urinary incontinence, which includes both stress and urgency urinary incontinence, adversely affects quality of life and can be difficult to manage. Studies comparing procedural-based treatments for mixed urinary incontinence are lacking.

**OBJECTIVE** To determine whether intradetrusor onabotulinumtoxinA is more effective than midurethral sling for the treatment of mixed urinary incontinence in females.

**DESIGN, SETTING, AND PARTICIPANTS** Randomized, superiority trial involving females (aged  $\geq 21$  years) with moderate to severe bother from both stress and urgency urinary incontinence who had unsuccessful conservative treatments and oral medications. The study was conducted at 7 US sites with enrollment between July 2020 and September 2022; the last date of follow-up was December 29, 2023.

**INTERVENTIONS** Intradetrusor injection of onabotulinumtoxinA, 100 U (treatment focused on the urgency component), vs surgical synthetic mesh midurethral sling (treatment focused on the stress component). Recipients of onabotulinumtoxinA could receive an additional injection between 3 and 6 months. All participants could receive additional treatment (including crossover to the alternative treatment) between 6 and 12 months.

**MAIN OUTCOMES AND MEASURES** The primary outcome was change at 6 months in mixed incontinence symptoms as measured by the Urogenital Distress Inventory (UDI) total score (0-300 points; higher scores indicate worse symptoms; minimal clinically important difference, 26.1). Secondary outcomes included stress and irritative UDI subscores.

**RESULTS** Among 150 females randomized, 137 were treated, had postbaseline outcome data, and were included in the primary analysis (mean [SD] age, 59.0 [11.5] years). Both groups demonstrated mean improvement in UDI total score at 6 months with no significant difference between groups (onabotulinumtoxinA: -66.8 points [95% CI, -84.9 to -48.8]; sling: -84.9 [95% CI, -100.5 to -69.3]; mean difference, 18.1 points [95% CI, -4.6 to 40.7];  $P = .12$ ). For secondary outcomes, greater UDI stress score improvement was seen with the sling (-45.2 [95% CI, -53.7 to -36.8]) compared with onabotulinumtoxinA (-25.1 [95% CI, -34.1 to -16.1]) ( $P < .001$ ); however, no significant difference was seen between groups in UDI irritative score (onabotulinumtoxinA: -32.9 [95% CI, -40.3 to -25.6] vs sling: -27.4 [95% CI, -34.6 to -20.3];  $P = .27$ ). In the onabotulinumtoxinA group, 12.7% and 28.2% received a second injection by 6 and 12 months, respectively. By 12 months, 30.3% in the sling group received onabotulinumtoxinA, and 15.5% in the onabotulinumtoxinA group received a sling. Overall, adverse events were not different between groups.

**CONCLUSIONS AND RELEVANCE** There was no observed difference in UDI total score improvement at 6 months between the onabotulinumtoxinA and midurethral sling groups in females with moderate to severe mixed urinary incontinence who previously did not respond to conservative treatments. These findings may help inform treatment decisions based on patient preference in partnership with clinician recommendations.

**TRIAL REGISTRATION** ClinicalTrials.gov Identifier: [NCT04171531](https://clinicaltrials.gov/ct2/show/study/NCT04171531)

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**M**ixed urinary incontinence (MUI), defined as involuntary leakage associated with urgency (ie, urgency urinary incontinence [UUI]) and with exertion, effort, sneezing, or coughing (ie, stress urinary incontinence [SUI]), is a common condition, and its prevalence increases with age.<sup>1,2</sup> In the US, MUI affects an estimated 30% of females 60 years of age and older, and the effect of MUI on quality of life can be profound, encompassing emotional, physical, economic, and social dimensions.<sup>1-4</sup> Females with urinary incontinence typically report that UUI is more bothersome than SUI, and the combination of both is more bothersome than either UUI or SUI alone.<sup>5-9</sup>

For females who had unsuccessful conservative approaches for MUI (ie, behavioral, pelvic floor muscle, and medication therapies) and want additional treatments, the benefits and order of approach of advanced bladder therapies (ie, procedural/surgical interventions) have been unclear. The historical approach of treating the UUI component first with either onabotulinumtoxinA or sacral neuromodulation does not ensure improvement in the SUI component. Similarly, until recently, there have been limited data on whether treating the SUI component with a midurethral sling would substantially improve the UUI component. The 2019 ESTEEM trial was among the first to address this question.<sup>10</sup> In this study, 416 women with MUI who sought surgical treatment for SUI were randomly assigned to either a combination of midurethral sling plus behavioral and pelvic floor muscle therapy or midurethral sling alone. While the sling procedure alone resulted in improvement of both SUI and UUI symptoms, those in the sling-only group had a higher likelihood of requiring additional treatment sooner.<sup>10</sup>

Fundamentally, the key question is not only what procedural treatment improves MUI symptoms the most, but also what is the best treatment to receive first because many patients eventually pursue both treatments. The current hypothesis hypothesized that treatment focused on the UUI component (onabotulinumtoxinA) would be superior to treatment focused on the SUI component (midurethral sling). The objective of the Treatment for Mixed Urinary Incontinence: Midurethral Sling vs Botox A (MUSA) trial was to determine whether intradetrusor injection of onabotulinumtoxinA (Botox A) would improve MUI symptoms in females at 6 months compared with midurethral sling.<sup>11</sup>

## Methods

### Study Design and Oversight

This was a multicenter, randomized, superiority trial approved by the institutional review boards of 7 clinical sites in the Eunice Kennedy Shriver National Institute of Child Health and Human Development Pelvic Floor Disorders Network. All participants provided written informed consent. Safety was reviewed by an independent data and safety monitoring board 3 times each year during the trial. Study methods have previously been published,<sup>11</sup> and the study protocol appears in [Supplement 1](#). The final statistical analysis plan appears in [Supplement 2](#). This study followed Consolidated Standards of Reporting Trials reporting guidelines.

### Key Points

**Question** Is there a superior procedural-based treatment for females with mixed urinary incontinence who have at least moderate bother from both stress and urgency incontinence?

**Findings** In this randomized clinical trial of 137 females with mixed urinary incontinence, there was no significant difference between onabotulinumtoxinA or midurethral sling in the change of the Urogenital Distress Inventory total score from baseline to 6 months after treatment. Both groups experienced improvement.

**Meaning** There were no observed differences in outcomes for females with mixed urinary incontinence undergoing treatment with onabotulinumtoxinA or midurethral sling. The study results support an approach that considers patient preference in partnership with clinician recommendations.

### Participants

Females were eligible if they were 21 years or older, reported moderate or severe bother from both SUI and UUI symptoms for at least 3 months, demonstrated a positive cough stress test (observed urine loss synchronous with a cough), documented at least 4 UUI episodes on a 3-day bladder diary, and had unsuccessful conservative treatments and oral medications. Exclusion criteria included anterior or apical prolapse at or beyond the hymen, planned concomitant surgery for anterior or apical prolapse, prior sling, current oral overactive bladder medication use (participants were eligible after a 3-week washout period), and postvoid residual volume greater than 150 mL on 2 occasions within the past 6 months or current urinary catheter use (eTable 1 in [Supplement 3](#)). Race and ethnicity data were collected to help describe the study population based on participant self-report from fixed US National Institutes of Health categories ([Figure 1](#) and [Table 1](#)).

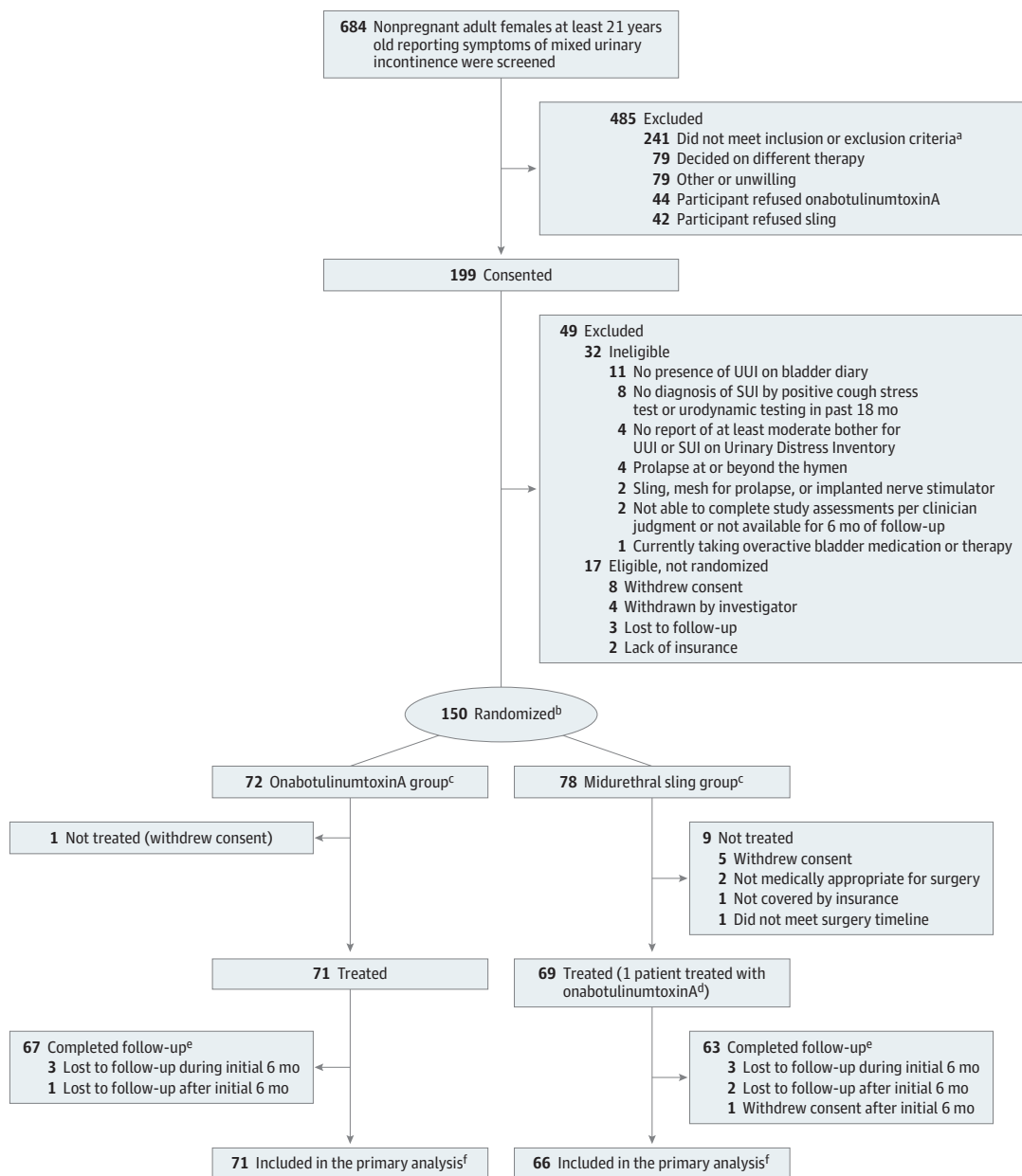
### Interventions and Randomization

Participants were randomly assigned to receive either intradetrusor injection of onabotulinumtoxinA, 100 U (office or operating room procedure), or synthetic polypropylene mesh midurethral sling (operating room procedure). Both retropubic and transobturator full-length midurethral sling techniques were allowed because previous trials support equivalent outcomes.<sup>12-15</sup> Consistent with the previous ESTEEM trial, single-incision midurethral slings were not included to better standardize the intervention.<sup>10</sup> Participants in the onabotulinumtoxinA group were eligible for an additional injection between 3 and 6 months. Participants in both groups had no urinary incontinence treatments other than the allocated study intervention for 6 months. After 6 months, all participants could cross over to the alternate treatment or request other treatments not included in the study. Participants were randomized 1:1 within the data management system using permuted blocks of sizes 2 and 4, stratified by clinical site and age ( $\geq 65$  or  $< 65$  years). Participants and surgeons were not masked. Outcome assessors were masked.

### Primary and Secondary Outcomes

All outcomes reported (primary, secondary, and exploratory) were prespecified. The study was powered for the primary out-

Figure 1. Participant Flow in the Treatment for Mixed Urinary Incontinence: Midurethral Sling vs Botox A Trial



SUI indicates stress urinary incontinence; UUI, urgency urinary incontinence.

<sup>a</sup>Specific inclusion and exclusion criteria were not maintained for screening failures.

<sup>b</sup>Randomization was stratified by clinical site and age category ( $\geq 65$ ,  $<65$  years).

<sup>c</sup>OnabotulinumtoxinA is focused on treating UUI, and midurethral sling is focused on treating SUI.

<sup>d</sup>One patient was randomized to midurethral sling but received

onabotulinumtoxinA. This patient remained in the primary analysis population under midurethral sling, the treatment to which the patient was randomized.

<sup>e</sup>Completion indicates that the patient finished their final follow-up visit. One patient, randomized before the 12-month follow-up extension was added as a protocol amendment, was considered to have completed the study at 6 months.

<sup>f</sup>Treated and had postbaseline efficacy data.

come, change in MUI symptoms at 6 months, measured using the Urogenital Distress Inventory (UDI) long-form total score (range 0-300 points; minimal clinically important difference [MCID], 26.1).<sup>10,11,16</sup> The UDI is a validated patient-reported outcome questionnaire with 3 symptom subscales: irritative symp-

oms (urgency incontinence, frequency, nocturia, and urgency), stress incontinence, and obstructive symptoms. Each subscale ranges from 0 to 100 points, with higher scores indicating greater symptom severity.<sup>16</sup> Recognizing that females with MUI may be unable to determine their type of in-

Table 1. Demographics and Baseline Characteristics

Characteristic	No. (%)	
	OnabotulinumtoxinA (n = 71) <sup>a</sup>	Midurethral sling (n = 66) <sup>a</sup>
Age, mean (SD) [range], y	59.1 (11.4) [27-78]	59.0 (11.7) [33-87]
Race <sup>b</sup>		
Asian	2 (2.8)	0
Black/African American	10 (14.1)	10 (15.2)
Native Hawaiian or Other Pacific Islander	1 (1.4)	1 (1.5)
White	55 (77.5)	54 (81.8)
Unknown/not reported	3 (4.2)	1 (1.5)
Hispanic/Latina ethnicity, No./total (%) <sup>c</sup>	15/71 (21.1)	6/65 (9.1)
Education, highest level obtained was greater than high school, No./total (%)	46/68 (64.8)	32/63 (48.5)
Currently smoking	7 (9.9)	9 (13.6)
No. of vaginal deliveries, median (IQR)	2 (1-3)	2 (1-3)
Total No. of deliveries, median (IQR)	2 (1-3)	2 (2-3)
Menopausal status		
Pre	7 (9.9)	14 (21.2)
Post	56 (78.9)	49 (74.2)
Not sure	8 (11.3)	3 (4.5)
Currently using estrogen by prescription	21 (29.6)	18 (27.3)
BMI, mean (SD) <sup>d</sup>	34.3 (8.3)	35.0 (7.6)
Type of urinary incontinence <sup>e</sup>		
Stress predominant	3 (4.2)	4 (6.1)
Urge predominant	7 (9.9)	10 (15.2)
Balanced	61 (85.9)	52 (78.8)
Baseline incontinence episode daily frequency, mean (SD)	7.1 (4.1)	7.4 (4.0)
Time from baseline visit to treatment, mean (SD), d <sup>f</sup>	59.0 (38.5)	56.8 (43.4)
Median (IQR)	49 (36-75)	46 (27-76)
Treatment >90 d after baseline	7 (9.9)	10 (15.2)
Baseline UDI scores, mean (SD) <sup>g</sup>		
Total	187.6 (38.2)	180.9 (36.5)
Irritative	75.7 (16.6)	77.3 (15.4)
Stress	86.6 (18.4)	80.3 (21.9)

Abbreviations: BMI, body mass index; UDI, Urogenital Distress Inventory.

<sup>a</sup> The primary analysis population is defined as all participants who received any treatment and have postbaseline efficacy data, regardless of randomized treatment.

<sup>b</sup> Race categories were self-reported using check all that apply and specific closed options, including an unknown/not reported selection.

<sup>c</sup> Ethnicity categories were self-reported using select only one, specific closed option, including an unknown/not reported selection.

<sup>d</sup> BMI calculated as weight in kilograms divided by height in square meters.

<sup>e</sup> The type of urinary incontinence is defined by responses at baseline on the UDI to the urgency urinary incontinence (UUI) item "Do you experience urine leakage related to a feeling of urgency? If yes, how much does it bother you?"

and stress urinary incontinence (SUI) item "Do you experience urine leakage related to physical activity, coughing or sneezing? If yes, how much does it bother you?" Greater bother reported on the UUI item is classified as urge predominant, greater bother reported on the SUI item is classified as stress predominant, and equal bother reported is classified as balanced.

<sup>f</sup> Baseline refers to the time of the first UDI assessment completion, which is used to determine eligibility. Participants were expected to receive treatment within 91 days of completing their baseline UDI.

<sup>g</sup> The UDI total score ranges from 0 to 300, and the UDI irritative and stress scores range from 0 to 100, with higher scores indicating greater symptom severity.

continence episode or which component is more bothersome (UUI or SUI), we chose the UDI total score as the primary outcome to reflect overall MUI symptoms. Secondary outcomes included the change in UDI total score at 3 months and the changes in UDI stress (MCID, 5.4)<sup>10</sup> and irritative (MCID, 10.2)<sup>10</sup> subscale scores at 6 months.

### Other Outcomes

Prespecified exploratory outcomes included the change in UDI total, stress, and irritative scores at 12 months. Incontinence-

specific quality of life was measured using the Incontinence Impact Questionnaire, which ranges from 0 to 400 points with an MCID of 16 points; higher scores indicate worse quality of life.<sup>16,17</sup> Participants completed the Patient Global Impression of Improvement (PGI-I)<sup>18</sup> questionnaire (range, 1 [very much better] to 7 [very much worse], dichotomized for analysis into responses 1-2 [much better and very much better compared with all other categories]), the PGI of Severity (PGI-S)<sup>18</sup> (range, 1 [normal] to 4 [severe], dichotomized into responses 1-2 [normal and mild] compared with all other categories), and

the Patient Global Symptom Control (PGSC) (“This treatment has given me adequate control of my urinary leakage”; range, 1 [disagree strongly] to 5 [agree strongly]). Overactive bladder-specific questionnaires included the Overactive Bladder Questionnaire (OAB-q)<sup>19</sup> (contains symptom bother and health-related quality of life [OAB-q-HRQL] subscales; responses on 6-point Likert scales; range, 0-100 points; higher scores indicate more severe symptoms or better quality of life, respectively) and the OAB Treatment Satisfaction Questionnaire (OAB-SAT-q)<sup>20</sup> (responses on 4-, 5-, and 6-point Likert scales; range, 0-100 points; higher scores indicate greater satisfaction). Three-day bladder diary measures were collected, including the number of total, irritative, and stress incontinence episodes per day. All questionnaires were administered at 3, 6, 9, and 12 months. Visits at 9 and 12 months were completed via telephone call. Participants completed questionnaires in REDCap or paper and the bladder diary by paper.

Other outcomes included additional urinary incontinence treatments, clinically important complications, and adverse events.

### Statistical Analysis

A sample size of 146 participants (73 per group) was planned to obtain 90% power to detect a difference between groups for the UDI total score change from baseline at 6 months of 26.1, which is the published MCID for women with MUI from the ESTEEM trial, assuming a 2-sided  $\alpha$  of .05, SD of 46.5, and an expected 5% dropout.<sup>10,21</sup> Because females in both groups could cancel procedures, nontreated patients were removed from the evaluation of efficacy for the primary analysis, consistent with analyses for prior Pelvic Floor Disorders Network protocols. The primary outcome population included randomized and treated participants with postbaseline efficacy data.

A general linear mixed model for repeated measures estimated the change from baseline in continuous outcomes at 3, 6, 9, and 12 months with fixed effects for the treatment group, time as a categorical variable, site, baseline score, age category, and interaction between treatment group and time. Correlation between repeated measures on the same participant was modeled using an unstructured pattern separately within each treatment group. An analogous generalized logistic mixed model compared treatments for binary outcomes. No multiple comparison adjustments were made for multiple outcomes, so findings for secondary and exploratory outcomes are descriptive.

Because additional urinary treatment was expected to improve outcomes, a supportive per-protocol analysis of the UDI total, stress, and irritative scores set to missing any outcome measures at 3 and 6 months that occurred after additional treatments (not allowed in the protocol) and excluded a participant who received the alternate treatment instead of the one to which they were randomized. Because additional and crossover treatments were allowed after 6 months, 3 sensitivity analyses compared the groups for change in UDI total score at 9 and 12 months, each with outcomes after any additional treatment set to missing: (1) an extension of the per-protocol analysis and (2) multiple imputation under alternative missing data assumptions via both control-based imputation and tipping point imputation (see eMethods in Supplement 3).<sup>22</sup>

To compare with the UDI MCID from ESTEEM, the MCID for the UDI total, stress, and irritative scores for this population of females with MUI who had unsuccessful conservative treatments and oral medications were estimated using anchor-based and distribution-based methods.<sup>23-26</sup>

Our statistical approach was performed as originally specified in the statistical analysis plan (Supplement 2). Analyses were performed using SAS version 9.4 (SAS Institute Inc). Statistical significance was set at  $P$  less than .05, and testing was 2-sided.

## Results

### Study Population

Between July 2020 and September 2022, 150 females were randomized, 140 were treated (onabotulinumtoxinA: 71 of 72 [98.6%], sling: 69 of 78 [88.5%]), and 137 had postbaseline data; 134 completed 6-month follow-up (onabotulinumtoxinA: 68 of 71 [95.8%], sling: 66 of 69 [95.7%]), and 130 completed the 12-month follow-up (onabotulinumtoxinA: 67 of 71 [94.4%], sling: 63 of 69 [91.3%]) (Figure 1).

Baseline demographic and clinical characteristics are provided in Table 1. The mean (SD) age of participants was 59.0 (11.5) years (range, 27 to 87 years); self-identified race was 1.5% Asian, 14.6% Black/African American, 1.5% Native Hawaiian or Other Pacific Islander, 79.6% White, and 2.9% unknown/not reported and 15.3% reported Hispanic/Latina ethnicity. MUI severity based on the UDI total mean (SD) score was 184.3 (37.4), the mean (SD) daily total incontinence episodes was 7.2 (4.1), and based on the UII and SUI bother questions from the UDI, most females (82.5%) had MUI that was balanced between stress and urgency.

### Primary Outcome

Both groups demonstrated mean improvement in the UDI total score at 6 months with no significant difference between groups (onabotulinumtoxinA: -66.8 points [95% CI, -84.9 to -48.8]; sling: -84.9 [95% CI, -100.5 to -69.3]; mean difference, 18.1 points [95% CI, -4.6 to 40.7],  $P = .12$ ; Table 2, Figure 2A and B), demonstrating that onabotulinumtoxinA injection was not superior to midurethral sling as hypothesized. The supportive per-protocol analysis was consistent with the primary analysis (eTable 2.1 and eFigure 1.1 in Supplement 3).

### Secondary Outcomes

There was no difference between groups in the UDI total score at 3 months (4.7 points [95% CI, -18.5 to 27.9],  $P = .69$ ). The UDI irritative and stress scores improved in both groups at 6 months (Table 2, Figure 2C-F). Although the onabotulinumtoxinA group generally reported a decrease in the UDI irritative score above the MCID of 10.2 compared with sling at 3 months, there was no difference between groups by 6 months (onabotulinumtoxinA: -32.9 [95% CI, -40.3 to -25.6] vs sling: -27.4 [95% CI, -34.6 to -20.3]; mean difference, -5.5 [95% CI, -15.3 to 4.3],  $P = .27$ ). The sling group had greater UDI stress score improvement at 6 months (-45.2 [95% CI, -53.7 to -36.8])

Table 2. Primary and Secondary Efficacy Outcomes

Month	OnabotulinumtoxinA (n = 71)			Midurethral sling (n = 66)			OnabotulinumtoxinA vs midurethral sling	
	No. <sup>a</sup>	Mean (SD)	Estimated mean change from baseline (95% CI) <sup>b</sup>	No. <sup>a</sup>	Mean (SD)	Estimated mean change from baseline (95% CI) <sup>b</sup>	Estimated mean difference (95% CI) <sup>b</sup>	P value <sup>b</sup>
<b>UDI total score at 6 mo (primary outcome)<sup>c,d</sup></b>								
0 (Baseline)	71	187.6 (38.2)		66	180.9 (36.5)			
6 mo	64	112.2 (74.2)	-66.8 (-84.9 to -48.8)	65	92.4 (61.9)	-84.9 (-100.5 to -69.3)	18.1 (-4.6 to 40.7)	.12
<b>UDI total score (secondary time points of primary outcome)<sup>c,d</sup></b>								
3 mo	68	106.4 (71.3)	-76.7 (-94.0 to -59.5)	64	95.1 (66.2)	-81.4 (-98.6 to -64.2)	4.7 (-18.5 to 27.9)	.69
9 mo	56	121.5 (68.9)	-55.3 (-72.6 to -38.1)	56	94.4 (63.2)	-79.6 (-96.8 to -62.5)	24.3 (1.1 to 47.5)	.04
12 mo	61	117.4 (70.4)	-60.5 (-77.5 to -43.4)	60	89.3 (67.3)	-84.9 (-102.4 to -67.3)	24.4 (1.1 to 47.7)	.04
<b>UDI irritative score (secondary outcome)<sup>c,e</sup></b>								
0 (Baseline)	71	75.7 (16.6)		66	77.3 (15.4)			
3 mo	68	35.1 (30.8)	-38.9 (-45.4 to -32.3)	64	49.3 (32.5)	-24.9 (-32.7 to -17.1)	-13.9 (-23.7 to -4.2)	.005
6 mo	64	40.1 (32.0)	-32.9 (-40.3 to -25.6)	65	46.6 (29.5)	-27.4 (-34.6 to -20.3)	-5.5 (-15.3 to 4.3)	.27
9 mo	56	42.2 (33.3)	-29.2 (-36.9 to -21.6)	56	46.0 (32.3)	-27.1 (-35.2 to -19.0)	-2.1 (-12.7 to 8.6)	.70
12 mo	61	43.2 (31.1)	-28.3 (-35.6 to -21.0)	60	43.7 (32.6)	-29.1 (-37.3 to -20.8)	0.8 (-9.8 to 11.3)	.89
<b>UDI stress score (secondary outcome)<sup>c,e</sup></b>								
0 (Baseline)	71	86.6 (18.4)		66	80.3 (21.9)			
3 mo	68	59.1 (37.4)	-24.2 (-33.5 to -14.9)	64	33.6 (34.7)	-46.6 (-55.6 to -37.7)	22.4 (10.0 to 34.8)	<.001
6 mo	64	56.8 (35.4)	-25.1 (-34.1 to -16.1)	65	35.6 (33.7)	-45.2 (-53.7 to -36.8)	20.1 (8.4 to 31.9)	<.001
9 mo	56	64.3 (32.9)	-17.2 (-26.0 to -8.4)	56	37.2 (35.0)	-41.2 (-51.2 to -31.1)	24.0 (11.2 to 36.7)	<.001
12 mo	61	62.0 (35.6)	-20.6 (-29.8 to -11.4)	60	34.4 (34.3)	-45.1 (-54.1 to -36.1)	24.5 (12.1 to 36.8)	<.001

Abbreviation: UDI, Urogenital Distress Inventory.

<sup>a</sup> The primary analysis population includes all participants who received any treatment and have postbaseline efficacy data, regardless of randomized treatment.

<sup>b</sup> Estimates and *P* values are from a general linear model for repeated measurements with fixed effects adjusting for baseline value, clinical site, age group ( $\geq 65$ ,  $<65$  years), treatment, month as a categorical predictor, and interaction between treatment and month, with an unstructured correlation pattern across months separately within each treatment group.

<sup>c</sup> The primary outcome is the UDI total score at 6 months. The 3 secondary

outcomes were the UDI total score at 3 months and the UDI irritative and stress scores at 6 months.

<sup>d</sup> The UDI total score ranges from 0 to 300; from the ESTEEM trial, the minimal clinically important difference for females with mixed urinary incontinence is 26.1 points, with higher scores indicating greater symptom severity.<sup>10</sup>

<sup>e</sup> The UDI subscales range from 0 to 100; from the ESTEEM trial, the minimal clinically important difference for females with mixed urinary incontinence is 10.2 points for irritative and 5.4 points for stress incontinence, with higher scores indicating greater symptom severity.<sup>10</sup>

than onabotulinumtoxinA (-25.1 [95% CI, -34.1 to -16.1]; mean difference, 20.1 [95% CI, 8.4 to 31.9]; *P* < .001), which is above the MCID of 5.4.

### Exploratory Outcomes

At the 12-month point, the difference between groups in the UDI total score widened (24.4 points [95% CI, 1.1 to 47.7], *P* = .04; Table 2) but was less than the MCID of 26.1. The UDI stress score continued to show greater improvement for the sling group compared with the onabotulinumtoxinA group (difference, 24.5 [95% CI, 12.1 to 36.8]; *P* < .001), and there continued to be no difference in UDI irritative score improvement between groups (0.8 points [95% CI, -9.8 to 11.3], *P* = .89). The prespecified supportive analysis confirmed the 12-month results (see eResults, eTables 2.1-2.3, and eFigures 1.1-1.2 in Supplement 3).

Both groups reported improvement in incontinence-specific symptoms, quality of life, and satisfaction, and most participants indicated satisfactory improvement and control of bladder symptoms at 6 and 12 months (eTable 3 and eFigure 2 in Supplement 3).

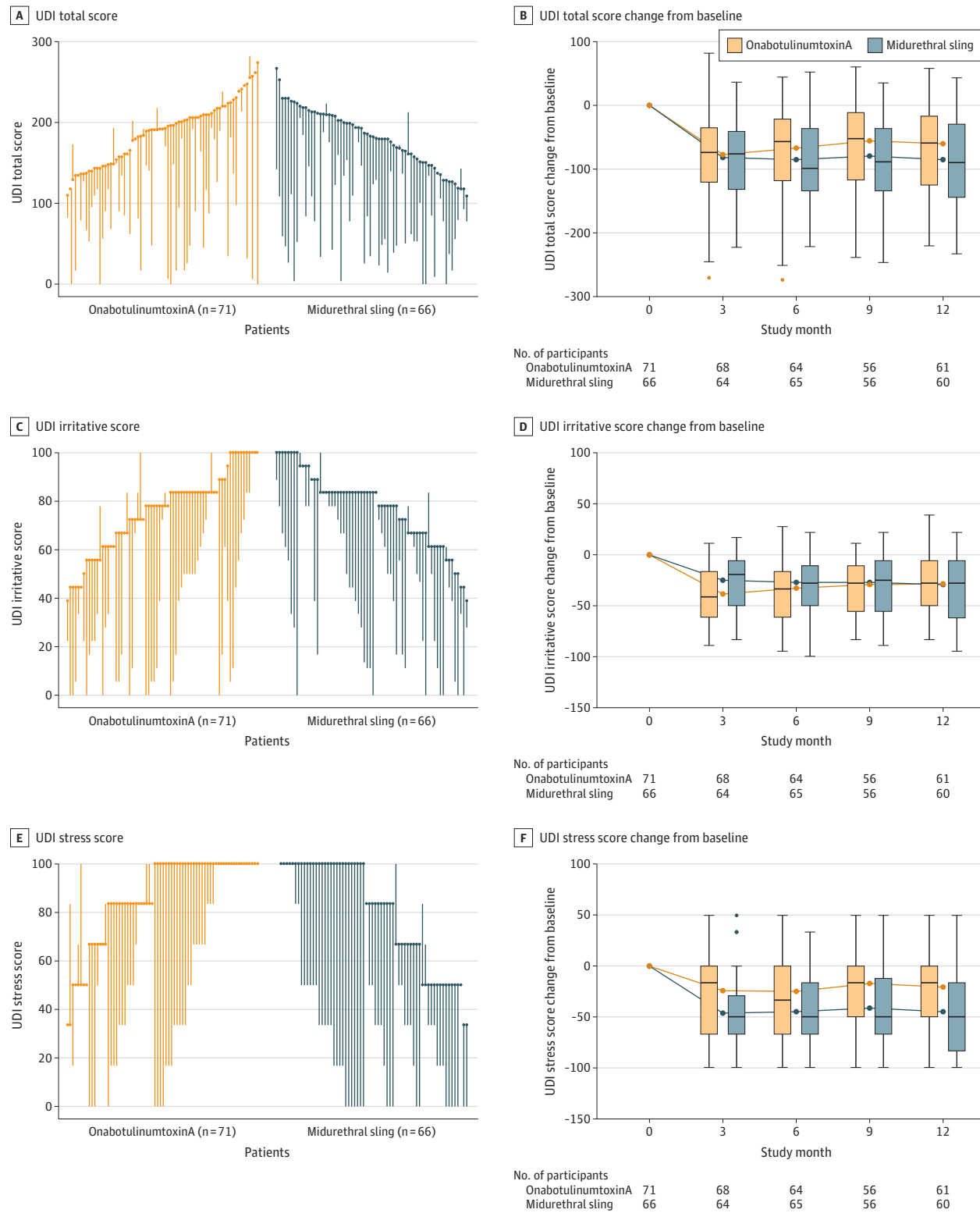
At 6 months, both groups had a reduction in total incontinence episodes per day (onabotulinumtoxinA: -2.9 [95%

CI, -3.6 to -2.1] vs sling: -4.0 [95% CI, -4.9 to -3.1]; difference, 1.1 [95% CI, 0.0 to 2.2]; *P* = .05). While there was no difference in reduction in irritative incontinence episodes per day between groups, the sling group had a greater reduction of stress incontinence episodes per day (difference, 0.9 [95% CI, 0.5 to 1.4], *P* < .001). By 12 months, there was no difference between groups in terms of reduction of stress, irritative, or total incontinence episodes per day (eTable 4 in Supplement 3).

### Additional Treatments

In the onabotulinumtoxinA group, 9 (12.7%) received a second injection by 6 months, and 20 (28.2%) received a second injection by 12 months. There was no difference in receipt of crossover treatment between groups at 6 months (onabotulinumtoxinA: 2.8% vs sling: 7.6%, *P* = .26); however, by 12 months, 20 (30.3%) in the sling group received onabotulinumtoxinA compared with 11 (15.5%) in the onabotulinumtoxinA group who received a sling (*P* = .04). In addition, throughout the study, 13.6% of participants in the sling group received nonstudy treatments compared with 7.0% in the onabotulinumtoxinA group (eTable 5 in Supplement 3).

Figure 2. Urogenital Distress Inventory (UDI) Total, Irritative, and Stress Scores Change From Baseline



UDI total score (range, 0-300), irritative subscale (range, 0-100), and stress subscale (range, 0-100) parallel line plot of observed change from baseline at 6 months by the baseline value, box plots, and model-estimated mean change from baseline at each time point. The minimal clinically important difference is 26.1 for the total score, 10.2 for the irritative subscale, and 5.4 for the stress

subscale. Boxplot midlines represent the median value, box ends represent quartile ranges, whiskers represent upper and lower limits at 1.5 times the IQR, and dots not on the lines indicate extreme values. Colored points represent model-estimated mean values.

**Table 3. Postoperative Complications and Adverse Events Within 12 Months in the Safety Population**

Complication <sup>a</sup>	No. (%)	
	OnabotulinumtoxinA (n = 72)	Midurethral sling (n = 68)
Any catheter placement or intermittent self-catheterization starting or continuing 2 or more wk after initial procedure	2 (2.8)	1 (1.5)
Went home with catheter at study intervention	0	8 (11.8)
Complications at time of study intervention <sup>b</sup>	0	2 (2.9)
Hospital admission or return to operating room related to intervention	0	0
Adverse events of special interest or related to pelvis within 12 mo		
Urinary tract infection	20 (27.8)	20 (29.4)
Pain <sup>c</sup>	20 (27.8)	15 (22.1)
Difficulty with bladder emptying <sup>d</sup>	15 (20.8)	22 (32.4)
Evidence of worsening urge incontinence <sup>e</sup>	15 (20.8)	11 (16.2)
Dyspareunia <sup>f</sup>	10 (13.9)	10 (14.7)
Recurrent urinary tract infection <sup>g</sup>	5 (6.9)	12 (17.6)
Pyelonephritis	1 (1.4)	1 (1.5)
Constipation	0	2 (2.9)
Midurethral sling mesh exposure	0	2 (2.9)
Midurethral sling removal/revision	0	1 (1.5)

<sup>a</sup> The safety population includes all participants who received any treatment, summarized by the actual treatment received.

<sup>b</sup> Complications in the midurethral group include 1 bladder injury and 1 vagotomy.

<sup>c</sup> Pain includes reported adverse events coded to MedDRA preferred term of *pelvic pain* or *lavator spasm* or a positive response to Urogenital Distress Inventory (UDI) item "Do you experience pain in the lower abdominal or genital area?"

<sup>d</sup> Difficulty with bladder emptying includes reported adverse events coded to Medical Dictionary for Regulatory Activities (MedDRA) preferred term of *urinary retention* or *residual urine volume* or a positive response to UDI item "Do you experience difficulty emptying your bladder?"

<sup>e</sup> Evidence of worsening urge incontinence was evaluated at all postbaseline visits, defined as any UDI irritative score increasing >12 points from baseline or any bladder diary average daily urge incontinence episode frequency increasing  $\geq 2$  episodes per day from baseline.

<sup>f</sup> Dyspareunia includes reported adverse events coded to MedDRA preferred term of *dyspareunia* or *partner dyspareunia* or a positive response to Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire-Revised version item "How often do you feel pain during sexual intercourse?"

<sup>g</sup> Recurrent urinary tract infection was reported by the investigator and confirmed by an independent medical monitor review.

### Complications and Adverse Events

Few complications were related to the interventions (Table 3; eTable 6 in Supplement 3). Serious adverse events (4.2% in the onabotulinumtoxinA group and 11.8% in the sling group) were unrelated to study treatments. For the initial randomized study intervention, no patient went home with a urinary catheter after onabotulinumtoxinA injection compared with 8 (11.8%) after a sling, and 2.8% and 1.5% required clean intermittent catheterization 2 weeks after onabotulinumtoxinA and sling,

respectively. Through 12 months, more participants in the sling group experienced recurrent urinary tract infections (17.6%) compared with the onabotulinumtoxinA group (6.9%). In the sling group, vaginal mesh exposure (mesh visible or palpable in the vagina that can cause vaginal bleeding, discharge, infection, pain, or dyspareunia) occurred in 2.9% and 1.5% required sling surgical revision. Worsening UUI from baseline at any time occurred in 20.8% and 16.2% of the onabotulinumtoxinA and sling groups, respectively.

### MCID Estimates From Study Data

MCID estimates for this study population were based on the mean of the distribution-based estimate and the anchor-based estimates using the PGI-I, PGSC, and number of daily incontinence episodes, resulting in MCIDs (in whole numbers) of 19 for the UDI total, 11 for the UDI irritative, and 9 for the UDI stress scores (eTables 7.1-7.4 in Supplement 3).

### Discussion

In this randomized trial of females with moderate to severe MUI who did not respond to conservative therapy and medications, onabotulinumtoxinA was not superior to midurethral sling. MUI symptoms improved in both groups at 6 months.

Secondary outcomes were selected to evaluate the UUI and SUI components of MUI after treatment with onabotulinumtoxinA (therapy focused on UUI) and midurethral sling (therapy focused on SUI). Participants receiving a midurethral sling had greater SUI symptom improvement than those receiving onabotulinumtoxinA at 6 months, but there were no differences in UUI symptom improvement. Bladder diary outcomes had a similar pattern of results at 6 months, with a greater reduction of SUI incontinence episodes in the sling group and no difference in the reduction of UUI incontinence episodes. One explanation for why a greater improvement in UUI outcomes was not seen in the onabotulinumtoxinA group compared with the sling group beyond 3 months is that onabotulinumtoxinA effects dissipate over time and while the onabotulinumtoxinA group participants were eligible for a second injection between 3 and 6 months, only 12.7% elected to do so. By 12 months, no differences were seen in UUI, SUI, or MUI symptoms or bladder diary results. This may be because 30.3% of the sling group and 15.5% of the onabotulinumtoxinA group received both therapies by 12 months.

The midurethral sling group had improvement in UUI symptoms at 6 months before they were allowed additional treatments. These improvements in UUI symptoms after a sling were also seen in the ESTEEM study, a trial of women with MUI that compared combined sling plus behavioral/pelvic floor muscle therapy vs sling alone.<sup>10</sup> Both groups in ESTEEM reported reductions in urgency symptoms. However, compared with the current study, where 30.3% of the sling group added onabotulinumtoxinA therapy by 12 months, only 12% in the ESTEEM study added UUI therapy. One explanation may be that the ESTEEM participants may represent a different MUI population who were not actively seeking treatment for bothersome UUI and were not required to have had unsuccessful

conservative treatment and oral medication, which was an eligibility criterion for the current trial.

In this group of females with moderate to severe MUI who had unsuccessful conservative therapy and medications, a portion required additional treatment to maintain clinical benefits beyond 6 months. By 12 months, 22.6% received both a sling and onabotulinumtoxinA, 10.2% received other nonstudy treatments, and 28.2% in the onabotulinumtoxinA group had a second injection. There was a higher proportion of patients in the sling group who received crossover treatment with onabotulinumtoxinA compared with those in the onabotulinumtoxinA group treated with a sling (30.3% vs 15.5%, respectively). Because sling procedures were performed in the operating room and onabotulinumtoxinA was primarily clinic based, participants may be more likely to undergo an additional, less-invasive procedure. However, this difference in crossover treatment could also be related to UI being more chronic, less predictable, and more bothersome than SUI. Thus, females may continue to seek additional treatment for UI symptoms.

Both treatments have risks associated with their use. The sling group had a similar rate of sling surgical revision (1.5%), vaginal mesh exposure (2.9%), and short-term postprocedural urinary catheter use (11.8%) compared with other studies.<sup>13,15,27</sup> No patients in the onabotulinumtoxinA cohort required immediate catheter use, although 2.8% required intermittent self-catheterization 2 weeks after the procedure, similar to published rates of 5%.<sup>28</sup> Urinary tract infections are common after both procedures and were consistent with prior studies.<sup>10,29</sup> There were no serious adverse events related to the study treatments.

The strengths of this study include a randomized design, validated patient-reported outcomes, and a staff that was masked to administer questionnaires and bladder diaries. In-

cluding a 6-month period limited to the randomized study intervention and a subsequent 6-month period allowing additional urinary incontinence treatments permit comparison of the study interventions and pragmatic evaluation of the need for additional MUI therapies.

### Limitations

This study has several limitations. First, participants and surgeons were not masked. Second, given counseling about possibly receiving the alternative intervention after 6 months, participants may have anticipated receiving both treatments, contributing to the crossover rate. However, this would have affected both groups equally, and the crossover rate was lower in the onabotulinumtoxinA group. Third, because MUI is a chronic condition, longer follow-up is needed to determine whether additional participants would cross over to the alternative treatment and the frequency of additional onabotulinumtoxinA injections. Fourth, this population is not representative of the distribution of race and ethnicity in the US.

### Conclusions

Among females with moderate to severe MUI who previously did not respond to conservative treatments and oral medications, onabotulinumtoxinA injection and midurethral sling surgery resulted in no observed difference in MUI symptom improvement at 6 months. Moderate to severe bothersome stress and urgency incontinence can be difficult to treat with one therapy, as 22.6% received both a sling and onabotulinumtoxinA by 12 months. These findings may help inform treatment decisions based on patient preference in partnership with clinician recommendations.

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## REFERENCES

- Haylen BT, de Ridder D, Freeman RM, et al; International Urogynecological Association; International Continence Society. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. *NeuroUrol Urodyn*. 2010;29(1):4-20. doi:10.1002/nau.20798
- Abufaraj M, Xu T, Cao C, et al. Prevalence and trends in urinary incontinence among women in the United States, 2005-2018. *Am J Obstet Gynecol*. 2021;225(2):166.e1-166.e12. doi:10.1016/j.ajog.2021.03.016
- Frick AC, Huang AJ, Van den Eeden SK, et al. Mixed urinary incontinence: greater impact on quality of life. *J Urol*. 2009;182(2):596-600. doi:10.1016/j.juro.2009.04.005
- Datar M, Pan LC, McKinney JL, Goss TF, Pulliam SJ. Healthcare resource use and cost burden of urinary incontinence to United States payers. *NeuroUrol Urodyn*. 2022;41(7):1553-1562. doi:10.1002/nau.24989
- Coyne KS, Zhou Z, Thompson C, Versi E. The impact on health-related quality of life of stress, urge and mixed urinary incontinence. *BJU Int*. 2003;92(7):731-735. doi:10.1046/j.1464-410X.2003.04463.x
- Minassian VA, Devore E, Hagan K, Grodstein F. Severity of urinary incontinence and effect on quality of life in women by incontinence type. *Obstet Gynecol*. 2013;121(5):1083-1090. doi:10.1097/AOG.0b013e31828ca761
- Agarwal A, Eryuzlu LN, Cartwright R, et al. What is the most bothersome lower urinary tract symptom? individual- and population-level perspectives for both men and women. *Eur Urol*. 2014;65(6):1211-1217. doi:10.1016/j.eururo.2014.01.019
- Monz B, Chartier-Kastler E, Hampel C, et al. Patient characteristics associated with quality of life in European women seeking treatment for urinary incontinence: results from PURE. *Eur Urol*. 2007;51(4):1073-1081. doi:10.1016/j.eururo.2006.09.022
- Dooley Y, Lowenstein L, Kenton K, FitzGerald M, Brubaker L. Mixed incontinence is more bothersome than pure incontinence subtypes. *Int Urogynecol J Pelvic Floor Dysfunct*. 2008;19(10):1359-1362. doi:10.1007/s00192-008-0637-4
- Sung VW, Borello-France D, Newman DK, et al; NICHD Pelvic Floor Disorders Network. Effect of behavioral and pelvic floor muscle therapy combined with surgery vs surgery alone on incontinence symptoms among women with mixed urinary incontinence: the ESTEEM randomized clinical trial. *JAMA*. 2019;322(11):1066-1076. doi:10.1001/jama.2019.12467
- Harvie HS, Richter HE, Sung VW, et al; NICHD Pelvic Floor Disorders Network. Trial design for mixed urinary incontinence: midurethral sling versus botulinum toxin A. *Urogynecology (Phila)*. 2024;30(5):478-488. doi:10.1097/SPV.0000000000001422
- Ford AA, Rogerson L, Cody JD, Aluko P, Ogah JA. Mid-urethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev*. 2017;7(7):CD006375. doi:10.1002/14651858.CD006375.pub4
- Barber MD, Kleeman S, Karram MM, et al. Transobturator tape compared with tension-free vaginal tape for the treatment of stress urinary incontinence: a randomized controlled trial. *Obstet Gynecol*. 2008;111(3):611-621. doi:10.1097/AOG.0b013e318162f22e
- Moalli PA, Pappas N, Menefee S, Albo M, Meyn L, Abramowitch SD. Tensile properties of five commonly used mid-urethral slings relative to the TVT. *Int Urogynecol J Pelvic Floor Dysfunct*. 2008;19(5):655-663. doi:10.1007/s00192-007-0499-1
- Richter HE, Albo ME, Zyczynski HM, et al; Urinary Incontinence Treatment Network. Retropubic versus transobturator midurethral slings for stress incontinence. *N Engl J Med*. 2010;362(22):2066-2076. doi:10.1056/NEJMoa0912658
- Shumaker SA, Wyman JF, Uebersax JS, McClish D, Fantl JA; Continence Program in Women (CPW) Research Group. Health-related quality of life measures for women with urinary incontinence: the Incontinence Impact Questionnaire and the Urogenital Distress Inventory. *Qual Life Res*. 1994;3(5):291-306. doi:10.1007/BF00451721
- Barber MD, Spino C, Janz NK, et al; Pelvic Floor Disorders Network. The minimum important differences for the urinary scales of the Pelvic Floor Distress Inventory and Pelvic Floor Impact Questionnaire. *Am J Obstet Gynecol*. 2009;200(5):580.e1-580.e7. doi:10.1016/j.ajog.2009.02.007
- Yalcin I, Bump RC. Validation of two global impression questionnaires for incontinence. *Am J Obstet Gynecol*. 2003;189(1):98-101. doi:10.1067/mob.2003.379
- Coyne KS, Matza LS, Thompson CL. The responsiveness of the Overactive Bladder Questionnaire (OAB-q). *Qual Life Res*. 2005;14(3):849-855. doi:10.1007/s11136-004-0706-1
- Margolis MK, Fox KM, Cerulli A, Arieli R, Kahler KH, Coyne KS. Psychometric validation of the overactive bladder satisfaction with treatment questionnaire (OAB-SAT-q). *NeuroUrol Urodyn*. 2009;28(5):416-422. doi:10.1002/nau.20672
- McGlothlin AE, Lewis RJ. Minimal clinically important difference: defining what really matters to patients. *JAMA*. 2014;312(13):1342-1343. doi:10.1001/jama.2014.13128
- O'Kelly M, Ratitch B. Analyses under missing-not-at-random assumptions. In: O'Kelly M, Ratitch B, eds. *Clinical Trials With Missing Data: A Guide for Practitioners*. John Wiley & Sons Inc; 2014:chap 7. doi:10.1002/9781118762516.ch7
- Crosby RD, Kolotkin RL, Williams GR. Defining clinically meaningful change in health-related quality of life. *J Clin Epidemiol*. 2003;56(5):395-407. doi:10.1016/S0895-4356(03)00044-1
- Revicki D, Hays RD, Cella D, Sloan J. Recommended methods for determining responsiveness and minimally important differences for patient-reported outcomes. *J Clin Epidemiol*. 2008;61(2):102-109. doi:10.1016/j.jclinepi.2007.03.012
- Guyatt GH, Osoba D, Wu AW, Wyrwich KW, Norman GR; Clinical Significance Consensus Meeting Group. Methods to explain the clinical significance of health status measures. *Mayo Clin Proc*. 2002;77(4):371-383. doi:10.4065/77.4.371
- Wyrwich KW, Bullinger M, Aaronson N, Hays RD, Patrick DL, Symonds T; Clinical Significance Consensus Meeting Group. Estimating clinically significant differences in quality of life outcomes. *Qual Life Res*. 2005;14(2):285-295. doi:10.1007/s11136-004-0705-2
- Tunitsky-Biton E, Murphy A, Barber MD, Goldman HB, Vasavada S, Jelovsek JE. Assessment of voiding after sling: a randomized trial of 2 methods of postoperative catheter management after midurethral sling surgery for stress urinary incontinence in women. *Am J Obstet Gynecol*. 2015;212(5):597.e1-597.e9. doi:10.1016/j.ajog.2014.11.033
- Visco AG, Brubaker L, Richter HE, et al; Pelvic Floor Disorders Network. Anticholinergic therapy vs onabotulinumtoxinA for urgency urinary incontinence. *N Engl J Med*. 2012;367(19):1803-1813. doi:10.1056/NEJMoa1208872
- 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):1366-1374. doi:10.1001/jama.2016.14617