




Treatment patterns in women with urinary urgency and/or urgency urinary incontinence in the symptoms of Lower Urinary Tract Dysfunction Research Network Observational Cohort Study

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Abstract

Background: Limited epidemiological data exist describing how patients engage with various treatments for overactive bladder (OAB). To improve care for patients with OAB, it is essential to gain a better understanding of how patients interface with OAB treatments longitudinally, that is, how often patients change treatments and the pattern of this treatment change in terms of escalation and de-escalation.

Objectives: To describe treatment patterns for women with bothersome urinary urgency (UU) and/or urgency urinary incontinence (UUI) presenting to specialty care over 1 year.

Study Design: The Symptoms of Lower Urinary Tract Dysfunction Research Network (LURN) study enrolled adult women with bothersome UU and/or UUI seeking care for lower urinary tract symptoms (LUTS) between January 2015 and September 2016. An ordinal logistic regression model was fitted to describe the probabilities of escalating or de-escalating level of treatment during 1-year follow-up.

Results: Among 349 women, 281 reported UUI and 68 reported UU at baseline. At the end of 1 year of treatment by a urologist or urogynecologist, the highest level of treatment received by participants was 5% expectant management, 36% behavioral treatments (BT), 26% physical therapy (PT), 26% OAB medications, 1% percutaneous tibial nerve stimulation, 3% intradetrusor onabotulinum toxin A injection, and 3% sacral neuromodulation. Participants using BT or PT at baseline were more likely to be de-escalated to no treatment

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than participants on OAB medications at baseline, who tended to stay on medications. Predictors of the highest level of treatment included starting level of treatment, hypertension, UUI severity, stress urinary incontinence, and anticholinergic burden score.

Conclusions: Treatment patterns for UU and UUI are diverse. Even for patients with significant bother from OAB presenting to specialty clinics, further treatment often only involves conservative or medical therapies. This study highlights the need for improved treatment algorithms to escalate patients with persistent symptoms, or to adjust care in those who have been unsuccessfully treated.

KEYWORDS

discontinuation, therapy, treatment outcome, urge incontinence, urgency

1 | INTRODUCTION

The lifetime prevalence of overactive bladder syndrome (OAB) in women is approximately 30%.¹ OAB encompasses lower urinary tract symptoms (LUTS) such as urinary urgency (UU), frequency, nocturia, and urgency urinary incontinence (UUI). Patients who report OAB symptoms are often managed with multiple treatments; however, similar to other chronic diseases,² patient willingness to try therapies with possible side effects or risks and adherence to treatments is poor with discontinuation rates of medications nearing 50% by the first month of treatment.³ Although several studies have reported an association between clinical improvement and treatment adherence, these studies need to be interpreted cautiously as this association may reflect treatment bias or compliance bias.^{4,5}

Limited epidemiological data exist describing how patients engage with various OAB treatments. Many factors, including patient, provider, payer, and treatment-effect, influence what kind of treatments patients are offered or have access to and when patients start, stop, or change treatments.^{6–9} To improve care for patients with OAB and identify potentially modifiable barriers to treatment, it is essential to gain a better understanding of how patients interface with OAB treatments longitudinally, that is, how often patients change treatments and the pattern of this treatment change in terms of escalation and de-escalation. Thus, the primary aim of this study was to describe the treatment patterns for UU and/or UUI women presenting to specialty care over 1 year using data from the Symptoms of Lower Urinary Tract Dysfunction Research Network (LURN).

2 | MATERIALS AND METHODS

2.1 | Study sample

LURN is a multicenter research network that performed a 1-year prospective observational cohort study of adults seeking specialty care, that is, care from a urogynecologist or urologist specializing in management of LUTS, between January 2015 and September 2016.¹⁰ Patients were eligible if they reported at least one urinary symptom in the past month based on the LUTS Tool and were seeking care from a LURN physician for the first time. The LUTS Tool comprises 44 questions on severity and bother of LUTS.^{11,12} Additional study inclusion and exclusion criteria have been previously published.¹³ After a baseline visit, participants were contacted for a follow-up visit every 3 months for 1 year. This study was approved by the Institutional Review Board at each site and written informed consent was obtained from all participants before enrollment.

The current study only included those women who reported bothersome UU or UUI. Participants with UU were identified if they reported a “sudden need to rush to urinate” (Q6 on the LUTS Tool) or a “sudden need to rush to urinate for the fear of leaking” (Q12) during the past month, while participants were categorized as having UUI if they responded “sometimes,” “often,” or “always” on Q16b—“leaked urine in connection with a sudden need to rush to urinate.” Women were included in this cohort if they reported of “sometimes,” “often,” or “always” on the LUTS Tool and also reported bothersome UU or UUI which was defined as “somewhat,” “quite a bit,” or “a great deal” bothered.

2.2 | Treatment for LUTS

Participant-reported treatments for LUTS were collected at baseline and every 3 months for 1 year including start and stop dates for medications and procedure dates. Treatments of interest for this study included: (1) behavioral therapy (BT), (2) prescribed course of pelvic floor physical therapy (PT) with a trained therapist, (3) OAB medications, (4) percutaneous tibial nerve stimulation (PTNS), (5) intradetrusor onabotulinumtoxinA injection, and (6) sacral neuromodulation (SNM). These treatments were ordered from 1 to 6, respectively, reflecting existing recommended treatment paradigms from conservative to aggressive or from least procedurally intensive to most surgically intensive.¹⁴ Treatment grouping was also performed for BT and OAB medications and these are listed in Supplementary Table 1. Intradetrusor onabotulinumtoxinA was assumed to be effective for 6 months from the last procedure date. Participants on SNM were assumed to continue SNM therapy unless the device was removed.

2.3 | Outcomes

The primary outcomes for this study were treatment escalation and de-escalation from baseline to follow-up. Escalation was defined as an increase in treatment level (e.g. from level 1 = BT to level 3 = OAB medication), whereas de-escalation was defined as a decrease in treatment level (e.g., from level 3 = OAB medication to level 1 = BT).

2.4 | Independent variables

Demographic variables included age at study enrollment, race, and education. The following baseline clinical characteristics were also collected: (1) body mass index (BMI); (2) comorbidities (history of hypertension, diabetes, psychiatric diagnosis, stroke or transient ischemic attack [TIA], and hyperlipidemia); (3) use of diuretics; (4) anticholinergic burden (ACB) score¹⁵; (5) UU and UII symptom severity questions from the LUTS Tool; (6) stress urinary incontinence (average of LUTS Tool items related to leaking urine in connection with laughing, sneezing, or coughing, and in connection with physical activities, such as exercising or lifting a heavy object); (7) Patient-Reported Outcomes Measurement Information System (PROMIS) measures¹⁶ (gastrointestinal bowel incontinence and diarrhea, constipation, depression, anxiety, physical functioning, and sleep disturbance measures); (8) quality of life due to urinary symptoms

as measured by Q8 of the American Urological Association Symptom Index¹⁷; and (9) the Perceived Stress Scale.¹⁸

2.5 | Statistical analyses

The highest level of treatment at each visit was plotted in a lasagna plot to show treatment patterns over time. The percentage of participants with treatment escalation and de-escalation between visits were calculated and presented using bar charts. Denominators of these percentages were the number of participants with treatment data from two consecutive visits, and numerators were the number of participants who had treatment escalation or de-escalation. To obtain predicted probabilities of treatment escalation and de-escalation from baseline to study follow-up, we fit a multivariable ordinal logistic regression model predicting the highest level of treatment during study follow-up using baseline characteristics. The ordinal logistic regression model was used to obtain predicted probabilities of each level of treatment from one unified model. For each participant, escalation (de-escalation) probabilities were obtained by summing up the predicted probabilities of all higher (lower) levels of treatment from their baseline level of treatment.

Candidate predictors were selected with clinical input. Model selection used backward elimination. Covariates significant at 0.10 level were included in the final model. To adjust for baseline treatments, level of treatment at baseline and prior sling placement at baseline were included as predictors regardless of *p* value.

All statistical analyses were conducted using SAS software, version 9.4 (SAS Institute).

3 | RESULTS

Among the 545 women enrolled in LURN, 349 women presented with bothersome UU or UII; 281 had bothersome UII (i.e., OAB-wet), and 68 had bothersome UU alone (i.e., OAB-dry) at baseline (Table 1). Mean (\pm SD) age was 57 (\pm 15) years and participants were mostly white (80%) and non-Hispanic (95%). Mean (\pm SD) BMI was 31.6 (\pm 8.2) kg/m². Before or at the time of their baseline visit, 69% of participants reported undergoing BT and 13% reported PT (Table 1). At baseline, 10% were taking OAB medications (our data set cannot ascertain how many had previously tried these medications). Few participants had tried PTNS ($n = 1$), intradetrusor onabotulinumtoxinA ($n = 2$), or

TABLE 1 Patient characteristics at baseline

	Total (<i>n</i> = 349)	Urinary urgency with urgency incontinence (<i>n</i> = 281)	Urinary urgency without urgency incontinence (<i>n</i> = 68)
Demographics			
Age in years	57.1 (14.6)	57.6 (14.0)	54.9 (16.6)
Race^a			
Black/African American	48 (14%)	40 (14%)	8 (12%)
Other	22 (6%)	17 (6%)	5 (7%)
White	278 (80%)	223 (80%)	55 (81%)
Ethnicity			
Hispanic/Latina	12 (3%)	9 (3%)	3 (4%)
Non-Hispanic/Non-Latina	330 (95%)	265 (94%)	65 (96%)
Ethnicity unknown	7 (2%)	7 (2%)	0 (0%)
Education^a			
<HS Diploma/GED	9 (3%)	7 (3%)	2 (3%)
HS Diploma/GED	33 (10%)	29 (10%)	4 (6%)
Some college/tech school—no degree	92 (27%)	77 (28%)	15 (23%)
Associates degree	40 (12%)	31 (11%)	9 (14%)
Bachelor's degree	96 (28%)	81 (29%)	15 (23%)
Graduate degree	75 (22%)	54 (19%)	21 (32%)
Physical exam and clinical information			
BMI (kg/m ²) ^a	31.6 (8.2)	32.0 (8.4)	29.5 (6.6)
Current smoker ^a	29 (8%)	24 (9%)	5 (7%)
Former smoker ^a	95 (27%)	77 (28%)	18 (26%)
Number of alcoholic drinks per week in the past year^b			
Has not had alcohol in the past year	69 (20%)	55 (20%)	14 (21%)
0–3 drinks per week	222 (65%)	179 (65%)	43 (64%)
4–7 drinks per week	38 (11%)	30 (11%)	8 (12%)
≥ 8 drinks per week	13 (4%)	11 (4%)	2 (3%)
Hypertension ^a	139 (40%)	120 (43%)	19 (28%)
Diabetes	58 (17%)	46 (16%)	12 (18%)
Psychiatric diagnosis ^a	153 (44%)	130 (46%)	23 (34%)
History of stroke or TIA ^a	15 (4%)	13 (5%)	2 (3%)
Hyperlipidemia ^a	110 (32%)	88 (31%)	22 (32%)
On diuretics	52 (15%)	44 (16%)	8 (12%)
IPAQ^b			
Low activity	194 (57%)	161 (59%)	33 (50%)

(Continues)

TABLE 1 (Continued)

	Total (n = 349)	Urinary urgency with urgency incontinence (n = 281)	Urinary urgency without urgency incontinence (n = 68)
Moderate activity	43 (13%)	36 (13%)	7 (11%)
High activity	101 (30%)	75 (28%)	26 (39%)

LUTS treatment

Treatment before or at baseline (not mutually exclusive)

Behavioral therapy	240 (69%)	195 (69%)	45 (66%)
Pelvic floor physical therapy	47 (13%)	39 (14%)	8 (12%)
OAB medication ^c	36 (10%)	29 (10%)	7 (10%)
PTNS	1 (0%)	0 (0%)	1 (1%)
Botox	2 (1%)	2 (1%)	0 (0%)
SNM	1 (0%)	1 (0%)	0 (0%)
Sling	36 (10%)	28 (10%)	8 (12%)

Note: Table values are mean (SD) or percent (frequency).

Abbreviations: BMI, body mass index; GED, General Educational Development; HS, high school; IPAQ, International Physical Activity Questionnaire; LUTD, lower urinary tract disease; LUTS, lower urinary tract symptoms; OAB, overactive bladder; PTNS, percutaneous tibial nerve stimulation; SNM, sacral neuromodulation; TIA, transient ischemic attack.

^aMissing <2%.

^bMissing 2–5%.

^cOAB medication only included current medication use at baseline.

SNM surgeries ($n = 1$). Ten percent reported a history of previous sling surgery before baseline.

At baseline, the mean (\pm SD) overall LUTS Tool severity score was 47.7 (\pm 12.8) and was higher in the UUI cohort compared with UU-only cohort (difference [95% confidence interval, CI] = 9.7 [6.1–13.2], Table 2). UUI participants had more severe frequency (difference [95% CI] = 5.0 [0.1–9.9]), urgency (difference [95% CI] = 18.0 [14.3–21.7]), and incontinence symptoms (difference [95% CI] = 23.5 [18.9–28.1]) than UU-only participants, but they were similar on other LUTS. The PROMIS measures were all within $\frac{1}{2}$ SD (5 points) of the normative population mean of 50, except for PROMIS Physical Function for which the UUI participants had lower physical function than the normative population mean.

3.1 | Treatment patterns over time

Figure 1 shows the patterns of the highest level of treatment over time among the participants. Each row of this lasagna plot represents a participant who was followed for 12 months (x -axis). The type of treatment a participant receives during a given 3-month interval is denoted with a color (see legend for “Level of

Treatment”). For example, if a participant who is on BT at baseline initiates OAB medication between 3 and 6 months and stays on that treatment for the remainder of the study period, that participant would have a yellow colored row at baseline which would change to aqua at 3 months and remain aqua. If a participant underwent a sling procedure, this was indicated with a black dot. At baseline, 52% of participants reported BT, 11% PT, and 10% OAB medication as the highest level of treatment, while 26% ($n = 90$) had not tried or were not currently using any of the treatments of interest before or at the time of their baseline visit. The majority of these 90 participants were treated during study follow-up (highest level of treatment: 26% [$n = 23$] with BT, 28% [$n = 25$] with PT, and 27% [$n = 24$] with OAB medications). Among the 182 (52%) participants on BT at baseline, 25% ($n = 45$) discontinued BT and remained untreated during study follow-up; 32% ($n = 58$) continued BT, 19% ($n = 34$) escalated to PT, and 20% ($n = 36$) to OAB medication during the study follow-up. Among the 38 (11%) participants using PT at baseline, 26% ($n = 10$) discontinued PT and did not receive any other treatment during the study follow-up; 8% ($n = 3$) de-escalated to BT, 47% ($n = 18$) continued PT, and 8% ($n = 3$) escalated to an OAB medication during the study

TABLE 2 Patient-reported measures at baseline

	Total (<i>n</i> = 349)	Urinary urgency with urgency incontinence (<i>n</i> = 281)	Urinary urgency without urgency incontinence (<i>n</i> = 68)
Overall LUTS Tool ^{a, b} Score ^c	47.7 (12.8)	49.6 (12.6)	39.9 (10.5)
LUTS Tool Frequency Score ^d	55.8 (18.4)	56.8 (17.8)	51.8 (20.1)
LUTS Tool Post-micturition Score ^e	48.4 (26.0)	48.9 (26.2)	46.4 (25.0)
LUTS Tool Urgency Score ^d	65.0 (18.0)	68.5 (17.5)	50.5 (12.5)
LUTS Tool Voiding Difficulty Score ^f	28.3 (21.1)	28.7 (21.1)	26.8 (21.3)
LUTS Tool Pain Score ^d	16.3 (21.7)	16.3 (21.5)	16.2 (22.8)
LUTS Tool UI Score ^f	45.4 (19.3)	50.1 (16.6)	26.6 (17.6)
Quality of life due to urinary symptoms (0 = Delighted to 6 = Terrible) ^f	4.7 (1.1)	4.8 (1.1)	4.3 (1.2)
PROMIS ^g Depression (<i>T</i> score) ^d	50.4 (9.0)	50.9 (9.1)	48.2 (8.0)
PROMIS Anxiety (<i>T</i> score) ^d	51.4 (9.4)	51.6 (9.6)	50.4 (8.5)
PROMIS Physical Function (<i>T</i> score) ^d	45.7 (10.4)	45.0 (10.4)	48.6 (10.2)
PROMIS Sleep Disturbance (<i>T</i> score) ^d	51.9 (4.8)	52.0 (4.9)	51.4 (4.7)
PROMIS GI Diarrhea (<i>T</i> score) ^d	49.7 (9.6)	50.0 (9.7)	48.2 (9.5)
PROMIS GI Constipation (<i>T</i> score) ^f	52.2 (8.2)	52.2 (8.1)	51.9 (8.4)
Perceived Stress Scale ^f	13.7 (7.8)	13.9 (7.7)	12.8 (7.9)
PROMIS GI Bowel Incontinence (raw scale) ^f	5.6 (2.7)	5.7 (2.8)	5.2 (2.7)

Note: Table values are mean (SD). The LUTS Tool scores range from 0 to 100 and were created by combining responses to related symptom severity questions from the LUTS Tool and calculating the Euclidean length of the relevant questions as a measure of overall symptom severity. Higher score means more severity. PROMIS measures *T*-scores have a mean of 50 and a SD of 10 by definition and are centered on the US general population. The minimal clinically important differences (MCID) is 3 to 5 points in *T*-scores across PROMIS measures.

Abbreviations: GI, gastrointestinal; LUTS, lower urinary tract symptoms; PROMIS, Patient-Reported Outcomes Measurement Information System; GI, gastrointestinal; UI, urinary incontinence.

^aLUTS Tool.¹¹

^bSee Helmuth et al.¹⁹

^cMissing 17%.

^dMissing 2–5%.

^eMissing <2%.

^fMissing 5–10%.

^gPROMIS.¹⁶

follow-up. Among the 35 (10%) participants using an OAB medication at baseline, 80% (*n* = 28) continued use and 20% (*n* = 7) escalated to third-line treatments. Third-line treatments were the least commonly used mode of treatment with only 12 (3%) participants using intradetrusor onabotulinumtoxinA, 4 (1%) PTNS, and 11 (3%) SNM before baseline or during the study. Supporting Information: Figure 1 shows the treatment escalation and de-escalation patterns over the follow-up period.

Slings were placed in 10% (*n* = 36) of participants before baseline and in 11% (*n* = 40) during the study follow-up (mostly between baseline and 3 months).

A minority (2% [*n* = 6]) had slings placed both before and after baseline (Figure 1).

3.2 | Probability of treatment escalation and de-escalation over 12 months

Based on the ordinal logistic regression model of highest level of treatment (Supporting Information: 2), on average, participants with no OAB treatment at baseline had an 0.81 probability of escalating to Level 1 (BT) or above (1+), 0.57 probability of escalating to Level 2 (PT) or above (2+), 0.30 probability of escalating to Level 3

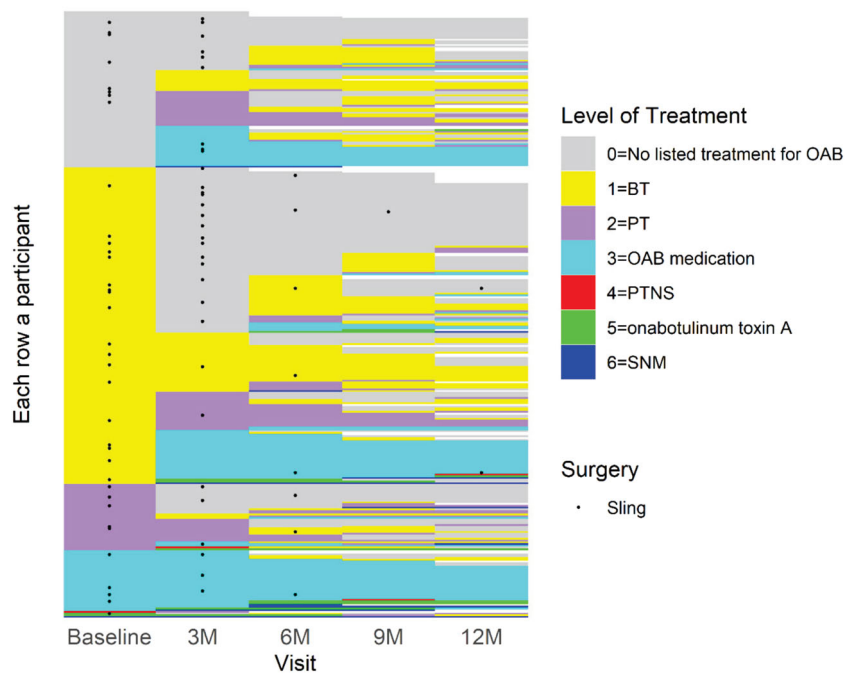


FIGURE 1 Lasagna plot of the highest level of treatment by visit. BT, behavioral therapy; OAB, overactive bladder; PT, pelvic floor physical therapy; PTNS, percutaneous tibial nerve stimulation; SNM, sacral neuromodulation.

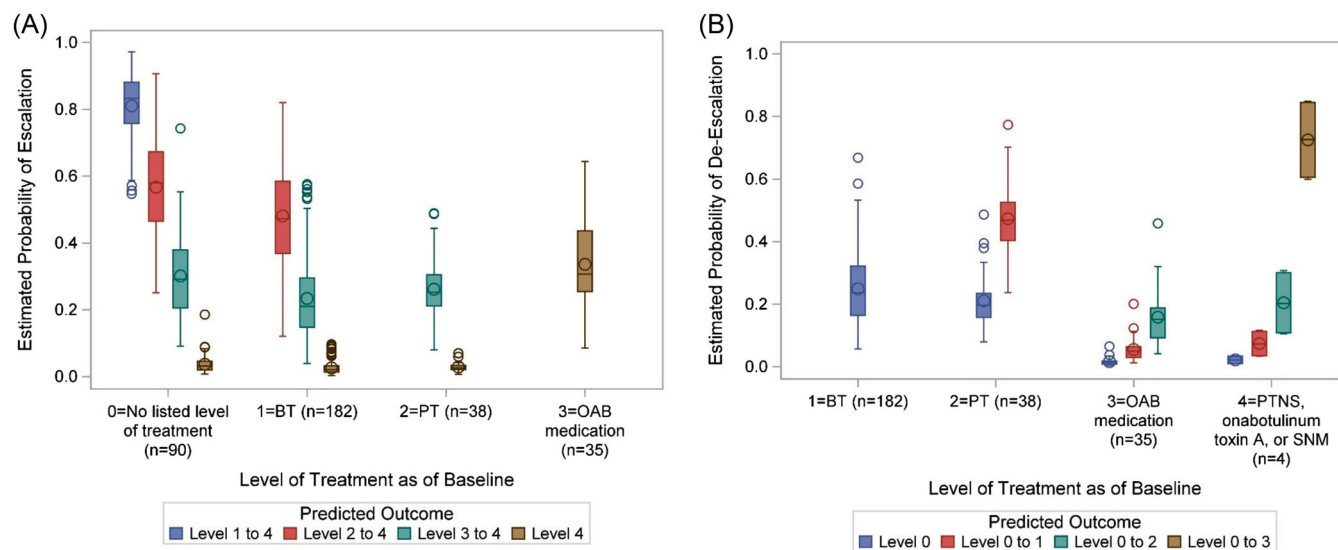


FIGURE 2 Estimated probability of (A) escalation and (B) de-escalation by level of treatment as of baseline. Results from proportional odds model. BT, behavioral therapy; PT, pelvic floor physical therapy; OAB, overactive bladder; PTNS, percutaneous tibial nerve stimulation; SNM, sacral neuromodulation.

(OAB medication) or above (3+), and 0.04 probability of escalating to Level 4 (surgeries/procedures) during the study period. Figure 2A represents these probabilities of escalating treatment visually. Participants were grouped based on their baseline treatment (*x*-axis). The distribution of estimated probabilities that they change treatment to a more invasive treatment is demonstrated by the box plots. For example, for participants who were not on any treatment at baseline (Level 0), the estimated average probability that they were escalated to a treatment of

Level 1 or greater (blue box plot) during the 1-year follow-up was 0.81. On average, participants on a Level 1 treatment (BT) at baseline had 0.48 probability of escalating to Level 2 or greater, 0.23 probability of escalating to Level 3 or greater, and 0.03 probability of escalating to Level 4. Participants on Level 2 (PT) at baseline had 0.26 probability of escalating to Level 3 or greater and 0.03 probability of escalating to 4. Finally, participants on Level 3 (OAB medication) at baseline had an average of 0.34 probability of escalating to Level 4.

Considering the probability of de-escalation (Figure 2B), participants on Level 1 (BT) at baseline had an average probability of 0.25 of de-escalating to Level 0 (no treatment). Participants on Level 2 (PT) at baseline had 0.47 probability of de-escalating to Level 1 or lower and 0.21 probability of de-escalating to Level 0. Participants on Level 3 (OAB medication) at baseline on average had 0.16 probability of de-escalating to Level 2 or lower, 0.06 probability of de-escalating to Level 1 or lower, and 0.02 probability of de-escalating to Level 0. Only four participants were on treatment Level 4 at baseline.

4 | COMMENT

4.1 | Principal findings

This study sought to elucidate patterns of treatment as well as factors associated with treatment escalation and de-escalation in a cohort of women with bothersome UU and UUI presenting to specialty care. Despite reporting significant bother from their OAB symptoms, approximately 40% of participants only received conservative treatment, that is, BT, or no treatment during the 12-month study period. Participants who were on OAB medications at baseline or were started on OAB medications after their first visit tended to stay on medications throughout the study period. Participants undergoing BT or PT at baseline were more likely to be de-escalated to no treatment than participants on OAB medications at baseline.

4.2 | Results in the context of what is known

Our study is the first to describe treatment patterns—escalation, de-escalation, and continuation—that incorporates all OAB treatment modalities in a cohort of women presenting to specialty care. Kraus et al.²⁰ described treatment patterns of patients with OAB over a 24-month period using a large, retrospective database. They defined their cohort by identifying patients who filled an OAB medication prescription or underwent a third-line procedure for OAB. Similar to our findings, they found that a small percentage (approximately 3%) of patients in the OAB medication cohort were escalated to a third-line treatment; however, of the patients in the third-line procedure cohort, one-third were prescribed an OAB medication. The study by Kraus et al. is limited by the reliance of medical claims to identify their patient cohort and thus does not capture patients with bothersome OAB who were undergoing more conservative

treatment options. Using a prospectively collected cohort of participants, our study demonstrated that a large proportion of patients who report bothersome UU and UUI only receive first-line treatments such as BT or no treatment at all, despite receiving care from a tertiary female urology or urogynecology clinic. In this study, we were also able to provide novel information regarding the average probability of treatment escalation or de-escalation depending on baseline characteristics. While these findings cannot fully account for the many reasons why escalation and de-escalation occur, they are able to increase awareness of how often they occur which can be useful information for patient counseling around treatment options.

Few studies have described the escalation to third-line treatments, but several studies have explored factors associated with discontinuation of third-line treatments. We were surprised to find that in our cohort of patients who sought care in tertiary academic medical centers, very few participants were escalated to third-line treatments during the study period; only 7% of participants were treated with any third-line treatments before baseline or during the study. In 2020, Kirby et al.²¹ performed a retrospective study using insurance claim data, exploring time to third-line treatment for women who were started on an OAB medication and found that the median time to receiving third-line treatment was 38 months from the first OAB medication prescription. In our cohort, 80% of participants who were on OAB medications at baseline continued medication during the study, while the remaining 20% were escalated to third-line treatments. It is possible that if we followed our cohort beyond 12 months that a greater proportion of patients would be escalated to third-line treatments. In 2021, Du et al.²² published a retrospective cohort study of new OAB patients presenting to a specialty care clinic to determine the impact of an OAB clinical care pathway on the rate of and time to third-line treatments. The clinical care pathway increased rates of third-line treatment from 7.7% to 13.4% at 6 months and 11.1% to 16.5% at 12 months while decreasing the time to third-line treatments from 280 to 160 days. Du et al.'s study highlighted the benefits of clinical care pathways yet underscored the fact that only a fraction of patients are escalated to third-line treatments, a similar finding in our study.

Many factors influence whether a patient continues or discontinues a given treatment. Prior studies have associated medication adherence with patient factors, such as age, weight, gender, symptom severity, cumulative ACB score, and comorbid conditions and treatment factors, such as adverse effects, cost, and efficacy.^{4,23–26} We identified several clinical factors associated with different treatment patterns. By pairing knowledge about

treatment patterns with patient clinical response and treatment goals, providers can improve their counseling around OAB treatments. Ultimately, data from this study can be used to create prediction tools that can assist providers individualize treatment plans with the goal to improve OAB symptoms.

4.3 | Strengths and limitations

To the best of our knowledge, our study is one of the first to describe treatment patterns for women with bothersome OAB that incorporate all OAB treatment modalities. This information could be used to develop clinical tools for counseling and refining treatment plans for patients, especially those at high risk for discontinuation of medication or conservative therapy. Other strengths include using data from a one year multicenter prospective observational study of patients seeking specialty care for LUTS. The generalizability of the study's findings is limited by the fact that the study cohort is mostly well-educated, English-speaking, and white participants seeking specialty care. Consequently, the findings may not be generalizable to other populations. Other limitations include participant recall bias, which could impact the reporting of symptom severity and treatments. Also, given the nature of the data available, we were not able to comment on several important factors that would impact treatment patterns. For instance, treatment cost, time constraints, side effects, and treatment response could impact a patient's ability or willingness to continue treatment, while limitations of insurance coverage, personal or group practice patterns, and medical training could influence a medical provider's ability or willingness to prescribe a given treatment. Furthermore, we were unable to capture participant satisfaction with treatment or response to treatments, which would greatly impact whether a patient is willing to continue to treatment or escalate therapy. It is possible that certain treatments were effective at treating the patient's bothersome symptoms, and thus escalation of treatment was not clinically indicated; conversely, those same treatments may not have been effective and thus were discontinued. Lastly, given the length of follow-up being restricted to 1 year, we may not have captured treatment escalation that had been planned or captured if longer longitudinal follow-up had been obtained.

4.4 | Clinical and research implications

The finding that so few patients with bothersome UU and/or UUI are escalated beyond conservative or

medication therapy is surprising given the percentage of patients who sought care after having tried these therapies already and reinforces the need for treatment algorithms that are centered on patient satisfaction and improved resolution of clinically bothersome symptoms. We also need to improve our understanding of treatment response as we are still uncertain if more prompt escalation to third-line treatments would lead to more impactful resolution of bothersome UU and UUI. Using these data to develop OAB treatment prediction tools would allow providers to individualize treatment plans and identify patients at risk for treatment discontinuation, as well as patients who may not be escalated to potentially beneficial OAB treatments with the goal to improve clinical outcomes for patients suffering from this chronic and often debilitating condition.

5 | CONCLUSIONS

Treatment patterns for UU and UUI are highly variable. Even for patients with significant bother from OAB presenting to specialty clinics, further treatment often only involves conservative or medical therapies. This study highlights the need for improved treatment algorithms to escalate patients with persistent symptoms or to adjust care in those who have been unsuccessfully treated.

AUTHOR CONTRIBUTIONS

Substantial contributions to conception and design, drafting and revising the article critically for important intellectual content, and final approval of the version to be published: Carol Emi Bretschneider, Qian Liu, Abigail R. Smith, Ziya Kirkali, Cindy L. Amundsen, Henry Lai, Juila Geynisman-Tan, Anna Kirby, Anne P. Cameron, Margaret E. Helmuth, James W. Griffith, John Eric Jelovsek.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in the NIDDK Central Repository at <https://repository.niddk.nih.gov/>; please reference the acronym "LURN."

ETHICS STATEMENT

All research is Institutional Review Board (IRB)-approved (IRB #14154-04). All human subjects provided written informed consent with guarantees of confidentiality. All human subjects provided written informed consent with guarantees of confidentiality.

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REFERENCES

1. Reynolds WS, Fowke J, Dmochowski R. The burden of overactive bladder on US public health. *Curr Bladder Dysfunct Rep.* 2016;11(1):8-13.
2. Brown MT, Bussell J, Dutta S, Davis K, Strong S, Mathew S. Medication adherence: truth and consequences. *Am J Med Sci.* 2016;351(4):387-399.
3. Yeowell G, Smith P, Nazir J, Hakimi Z, Siddiqui E, Fatoye F. Real-world persistence and adherence to oral antimuscarinics and mirabegron in patients with overactive bladder (OAB): a systematic literature review. *BMJ Open.* 2018;8(11):e021889.
4. Benner JS, Nichol MB, Rovner ES, et al. Patient-reported reasons for discontinuing overactive bladder medication. *BJU Int.* 2010;105(9):1276-1282.
5. Andy UU, Arya LA, Smith AL, et al. Is self-reported adherence associated with clinical outcomes in women treated with anticholinergic medication for overactive bladder? *NeuroUrol Urodyn.* 2016;35(6):738-742.
6. Kato D, Uno S, Van Schyndle J, Fan A, Kimura T. Persistence and adherence to overactive bladder medications in Japan: a large nationwide real-world analysis. *Int J Urol.* 2017;24(10):757-764.

7. Illiano E, Finazzi Agrò E, Natale F, Balsamo R, Costantini E. Italian real-life clinical setting: the persistence and adherence with mirabegron in women with overactive bladder. *Int Urol Nephrol*. 2020;52(6):1035-1042.
8. Kalder M, Pantazis K, Dinas K, Albert US, Heilmaier C, Kostev K. Discontinuation of treatment using anticholinergic medications in patients with urinary incontinence. *Obstet Gynecol*. 2014;124(4):794-800.
9. Athanasopoulos A, Giannitsas K. An overview of the clinical use of antimuscarinics in the treatment of overactive bladder. *Adv Urol*. 2011;2011:820816.
10. Yang CC, Weinfurt KP, Merion RM, Kirkali Z, LURN Study Group. Symptoms of Lower Urinary Tract Dysfunction Research Network. *J Urol*. 2016;196(1):146-152.
11. Coyne KS, Barsdorf AI, Thompson C, et al. Moving towards a comprehensive assessment of lower urinary tract symptoms (LUTS). *NeuroUrol Urodyn*. 2012;31(4):448-454.
12. Coyne KS, Sexton CC, Kopp Z, et al. Assessing patients' descriptions of lower urinary tract symptoms (LUTS) and perspectives on treatment outcomes: results of qualitative research. *Int J Clin Pract*. 2010;64(9):1260-1278.
13. Cameron AP, Lewicky-Gaupp C, Smith AR, et al. Baseline lower urinary tract symptoms in patients enrolled in LURN: a prospective, observational cohort study. *J Urol*. 2018;199(4):1023-1031.
14. Lightner DJ, Gomelsky A, Souter L, Vasavada SP. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU Guideline Amendment 2019. *J Urol*. 2019;202(3):558-563.
15. Carnahan RM, Lund BC, Perry PJ, Pollock BG, Culp KR. The Anticholinergic Drug Scale as a measure of drug-related anticholinergic burden: associations with serum anticholinergic activity. *J Clin Pharmacol*. 2006;46(12):1481-1486.
16. Cella D, Riley W, Stone A, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008. *J Clin Epidemiol*. 2010;63(11):1179-1194.
17. Barry MJ, Williford WO, Chang Y, et al. Benign prostatic hyperplasia specific health status measures in clinical research: how much change in the American Urological Association symptom index and the benign prostatic hyperplasia impact index is perceptible to patients? *J Urol*. 1995;154(5):1770-1774.
18. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav*. 1983;24(4):385-396.
19. Helmuth ME, Abigail RS, Andreev V, et al. Use of Euclidean length to measure urinary incontinence severity based on the lower urinary tract symptoms tool. *American Journal of Obstetrics & Gynecology*. 2017;218(3):357-359.
20. Kraus SR, Shiozawa A, Szabo SM, Qian C, Rogula B, Hairston J. Treatment patterns and costs among patients with OAB treated with combination oral therapy, sacral nerve stimulation, percutaneous tibial nerve stimulation, or onabotulinumtoxinA in the United States. *NeuroUrol Urodyn*. 2020;39(8):2206-2222.
21. Kirby AC, Park S, Cook SB, Odem-Davis K, Gore JL, Wolff EM. Practice patterns for women with overactive bladder syndrome: time between medications and third-line treatments. *Female Pelvic Med Reconstr Surg*. 2020;26(7):431-436.
22. Du C, Berg WT, Siegal AR, et al. A retrospective longitudinal evaluation of new overactive bladder patients in an FPMRS urologist practice: are patients following up and utilizing third-line therapies? *NeuroUrol Urodyn*. 2021;40(1):391-396.
23. Lua LL, Pathak P, Dandolu V. Comparing anticholinergic persistence and adherence profiles in overactive bladder patients based on gender, obesity, and major anticholinergic agents. *NeuroUrol Urodyn*. 2017;36(8):2123-2131.
24. Soda T, Tashiro Y, Koike S, Ikeuchi R, Okada T. Overactive bladder medication: persistence, drug switching, and reinitiation. *NeuroUrol Urodyn*. 2020;39(8):2527-2534.
25. Ivchenko A, Bödeker RH, Neumeister C, Wiedemann A. Anticholinergic burden and comorbidities in patients attending treatment with tropsium chloride for overactive bladder in a real-life setting: results of a prospective non-interventional study. *BMC Urol*. 2018;18(1):80.
26. Kim TH, Lee KS. Persistence and compliance with medication management in the treatment of overactive bladder. *Investig Clin Urol*. 2016;57(2):84-93.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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