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Sleep Disturbance Among Adults With Overactive Bladder: A Cross-sectional Survey

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OBJECTIVE	To examine differences in sleep disturbance, nocturia, and depression among adults with overactive bladder (OAB) by treatment type.
METHODS	A cross-sectional survey of adults with OAB assessed sleep disturbance, nocturia, and depression using patient-reported outcome measures, including the Patient Reported Outcomes Measurement Information System (PROMIS)-29 Profile v2.1 (Sleep Disturbance and Depression domains), Lower Urinary Tract Dysfunction Research Network Symptom Index-10, and PROMIS Sleep Disturbance Short Form 8B. Treatment groups included antimuscarinics, β-3 adrenergic agonists, and no treatment. Analysis of covariance (ANCOVA) was used to test for differences in study endpoints; Bonferroni-adjusted pairwise tests ($P < .05/3$) were performed to compare differences in least squares means between groups.
RESULTS	One hundred participants were included per treatment group. The overall mean (standard deviation) age across all groups was 47.8 (11.8) years. Symptom scores across all PROMIS domains in all three treatment groups were higher than the US general population. There were no statistically significant differences in outcomes across treatment groups.
CONCLUSION	Adults with OAB reported being affected by sleep disturbance and depression, regardless of treatment. The mirabegron group trended toward the lowest symptom impact across all outcomes, however, comparisons were not significant. Future research should examine temporal associations between OAB treatment, sleep disturbance, and outcomes. UROLOGY 179: 23–31, 2023. © 2023 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Overactive bladder (OAB) is a chronic urologic condition characterized by urinary urgency, with or without urgency urinary incontinence, accompanied by urinary frequency and nocturia.[1,2] The overall prevalence of OAB in the US ranges between 16.5% and 23.3%; most studies report a higher prevalence among women and among African Americans.[3] First-line therapy for OAB comprises behavioral intervention, followed by pharmacotherapies, including antimuscarinics, β-3 adrenergic agonists, and combination therapy.[4]

Nocturia, defined as nighttime awakening to void, is common in OAB.[5] Nocturia is strongly correlated with sleep disturbance, and associated with several adverse consequences, including decreased health-related quality of life (HRQoL) and increased morbidity and mortality.[6] Nocturia is frequently concurrent with depression, which is similarly associated with OAB.[7-9]

There is limited evidence characterizing the relationship between nocturia, sleep disturbance, and depression among OAB patients. Ge et al found that among a clinic-based sample of adults with OAB, sleep disturbance, and fatigue were greater than that of controls, and traced between-group differences in sleep disturbance to nocturia.[8] Additionally, sleep disturbance and fatigue were associated with depression, anxiety, and reduced HRQoL.[8] Another clinic-based study of patients with depression found that OAB occurred frequently, and was associated with lower sleep quality and risk of insomnia.[10]

The effect of OAB pharmacotherapy on sleep disturbance has not been completely investigated. One study (n = 15) investigating the antimuscarinic solifenacin reported reduced sleep disturbance due to decreased urinary urgency, and one trial (n = 34) investigating the β-3 adrenergic agonist mirabegron reported improvements in sleep disturbance due to reduced nocturia.[11,12] There are

currently no comparative data between antimuscarinics' and β-3 adrenergic agonists' effect on sleep disturbance.

The successful management of OAB symptoms could result in improved sleep, leading to improvements in patient well-being and HRQoL. The objectives of this study were to: (1) Examine differences in sleep disturbance (as measured by the Patient Reported Outcomes Measurement Information System 29 Profile, PROMIS-29); (2) Examine differences in depression (as measured by the PROMIS-29 Depression subscale); (3) Examine differences in sleep disturbance using the PROMIS Sleep Disturbance Short Form 8B; and (4) Examine differences in nocturia, as measured by the Lower Urinary Tract Dysfunction Research Network Symptom Index (LURN SI-10), among adults with OAB who are taking either mirabegron, antimuscarinics, or no treatment.

METHODS

Study Design and Population
This was a cross-sectional, noninterventional, nonrandomized, web-based survey of adults with OAB in the US. A convenience sample was recruited from patient panels maintained by Medicys, a professional patient recruitment vendor.

The target population for this study included three treatment groups: (1) current users of mirabegron, (2) current users of an antimuscarinic, and (3) untreated (including both nonusers and former users of OAB medications; "former use" was defined as no use of OAB medications for at least 3 months prior to the time of study recruitment). Participants were required to be aged 18-90 years, live in the US, have self-reported symptoms and/or self-reported diagnosis of OAB, and have been taking mirabegron or an antimuscarinic for at least 30 days, or have taken no OAB medication for at least 3 months prior to the time of recruitment. For the full list of inclusion and exclusion criteria, as well as the screening questions used to evaluate urinary symptoms, see Supplementary Materials.

The study period was from February to May 2022. All procedures complied with the current Health Insurance Portability and Accountability Act regulations. Institutional review board approval of the study protocol was obtained. Each participant provided consent prior to participation in the study. Pilot study participants were compensated $100; study participants were compensated $25. Study participation compensation was subsequently increased to $40 to improve response rate.

Survey Administration
Participants received email invitations with a unique web URL for survey access. Those who clicked on the survey link were interpreted as showing interest in the survey and thus considered "responders." Screening questions were administered to responders to verify study eligibility. A pilot study was conducted among 15 participants to assess survey feasibility. The final survey was completed independently by participants on the electronic survey platform.

Survey Content: Primary Outcomes
The PROMIS-29 Profile v2.1 was used to assess sleep disturbance and depression. The PROMIS-29 Profile is a 29-item measure that assesses physical functioning, anxiety, depression, fatigue, sleep disturbance, ability to participate in social roles and activities, pain interference, and pain intensity over a 7-day period.[13] Items are measured using a 5-point ordinal scale for all domains except pain intensity, which uses a numeric rating scale of 0-10. Higher scores indicate more of the concept being measured (eg, more sleep disturbance or worse depression). The sleep disturbance subscale includes 4 items measuring sleep quality, restoration, sleep problems, and difficulties falling asleep. The depression subscale includes 4 items measuring the frequency of feeling worthless, helpless, depressed, and hopeless. Raw scores for each item in these subscales were applied to a T-score metric with a mean of 50 and standard deviation (SD) of 10, thereby enabling comparison to the general population.[14]

The PROMIS Sleep Disturbance Short Form 8b 8-item scale was used to provide a more in-depth assessment of sleep disturbance. Items on the PROMIS Sleep Disturbance Short Form 8b assess sleep quality, sleep depth, satisfaction, and restoration over the past 7 days using 5-point ordinal scales; higher scores indicate worse outcomes.[15] Three items from the PROMIS Sleep Disturbance Short Form 8b are also included in the PROMIS-29 Profile and were only collected once within the survey. Raw scores for each item are standardized into T-scores.

The LURN SI-10 assesses nocturia and other lower urinary tract symptoms associated with OAB, including urinary urgency, urgency urinary incontinence, frequency, pain, and postmicturition symptoms.[16] Scores on the LURN SI-10 range from 0 to 38, with higher scores indicative of more severe symptoms. For the primary analyses, nocturia was assessed on the question: "In the past 7 days, during a typical night, how many times did you wake up and urinate?" Responses for this item are scored from 0 to 4, where 0 = None, 1 = 1 time, 2 = 2-3 times, and 4 = more than 3 times.

Survey Content: Other Patient-reported Outcomes
Other patient-reported outcomes assessed OAB symptom bother, depression, and sleep, primarily to serve as model covariates in statistical analyses. The Overactive Bladder Questionnaire Short Form (OAB-q SF) was administered to describe participant symptom bother and HRQoL during the past 4 weeks.[17] The OAB-q SF consists of 19 items measured using a 6-point ordinal scale. The OAB-q SF Symptom Bother and HRQoL domain scores range from 0 to 100, with a higher score corresponding to worse outcomes for symptom bother, but better outcomes for HRQoL. Participant demographics and clinical characteristics were also collected.
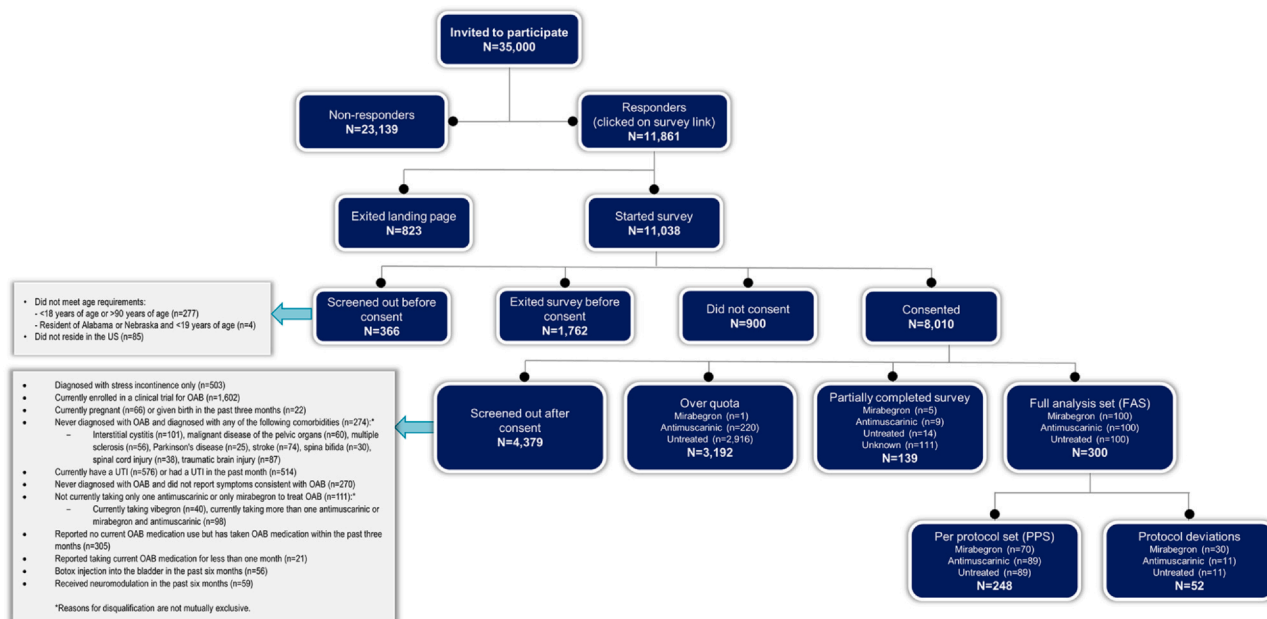
Figure 1. Flow diagram showing the response rate among all patients invited to participate in the study. (Color version available online.)

Statistical Analyses

Sample size was estimated using a level of significance of 5%, power of 80%, and analysis of covariance (ANCOVA) as the test type. A difference of 4 points on the PROMIS-29 sleep disturbance score between groups was considered clinically meaningful and resulted in a total sample size of N = 192 (96 participants per treatment group). Thus, 100 participants per treatment group (300 participants total) were targeted for the study sample.

For descriptive analyses, continuous data were summarized using the mean, SD, median, minimum, and maximum; categorical data were summarized by frequencies and percentages. ANCOVA models were used to test whether there were overall differences in study endpoints (mean PROMIS-29 sleep disturbance score, mean PROMIS-29 depression score, mean PROMIS Sleep Disturbance Short Form 8b score, and mean score on the LURN SI-10 nocturia item). Bonferroni-adjusted pairwise tests ($P < .05/3$) were performed to compare differences in least squares mean values between groups (mirabegron vs untreated, mirabegron vs antimuscarinic, and antimuscarinic vs untreated).

Covariates were included in the ANCOVA models after examining differences by treatment group. For each potential covariate, one-way ANOVA models assessed whether significant differences existed across groups; covariates were included if a significant difference was found ($P < .05$). Six covariates were identified a priori as candidates for inclusion in the models: age, sex, duration on current treatment, duration from symptom onset, depression (PGI-S), and OAB severity (OAB-q SF). Additional covariates were identified during the modeling exercise comparing differences by treatment group. No imputation was performed for missing data.

RESULTS

Survey Response Rate

Email invitations were sent to 35,000 patient panel members; of these, 11,861 individuals (33.9%) responded; 11,038 individuals (31.5% of invitees) started the survey (Fig. 1). The target population size of 300 participants was met. A further 3192 individuals (39.9% of 8010 consenting individuals) were excluded due to exceeding the target population size.

The full analysis set (FAS) included 300 patients, all of whom completed the informed consent, submitted a completed survey, and passed all quality control checks. Fifty-two (17.3%) patients who were in violation of the protocol (prior diagnosis with interstitial cystitis and/or malignant disease of the pelvic organs) were included in the FAS due to an error in the survey programming instructions. Sensitivity analyses were conducted to assess whether this impacted study conclusions (see "Sensitivity Analyses" below for details).

Participant Demographics and Clinical Characteristics

The mean (SD) age among participants was 47.8 (11.8) years (Table 1). Most participants were female (67.7%) and identified as White (84.7%). Among treatment groups, education varied significantly (P-value = .008); a larger proportion of participants taking mirabegron reported having a college degree (39.0%) or postgraduate degree (20.0%) compared to participants taking antimuscarinics (32.0% and 15.0%, respectively) or untreated participants (22.0% and 11.0%, respectively).

Table 1. Participant demographics by treatment group.

	Total (N = 300)	Treatment Group Mirabegron (N = 100)	Antimuscarinics (N = 100)	Untreated (N = 100)	P-Value[6]
Sex, n (%)					.0254
Male	97 (32.3%)	38 (38.0%)	22 (22.0%)	37 (37.0%)	
Female	203 (67.7%)	62 (62.0%)	78 (78.0%)	63 (63.0%)	
Ethnicity, n (%)					.1179
Hispanic or Latino	25 (8.3%)	13 (13.0%)	6 (6.0%)	6 (6.0%)	
Not Hispanic or Latino	275 (91.7%)	87 (87.0%)	94 (94.0%)	94 (94.0%)	
Race, n (%)					.8161
White	254 (84.7%)	86 (86.0%)	82 (82.0%)	86 (86.0%)	
Black or African American	27 (9.0%)	8 (8.0%)	11 (11.0%)	8 (8.0%)	
American Indian/Alaska Native	1 (0.3%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	
Asian or Asian American	2 (0.7%)	1 (1.0%)	0 (0.0%)	1 (1.0%)	
Middle Eastern	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Mixed Race	5 (1.7%)	1 (1.0%)	3 (3.0%)	1 (1.0%)	
Native Hawaiian/Pacific Islander	1 (0.3%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	
Other[1]	10 (3.3%)	3 (3.0%)	3 (3.0%)	4 (4.0%)	
Age (y)					.3557
n	300	100	100	100	
Mean	47.8	48.9	48.0	46.5	
SD	11.8	13.7	10.5	11.0	
Min	21	22	26	21	
Median	48.0	47.5	50.0	48.0	
Max	80	80	70	65	
Marital status, n (%)					.0426
Married/Domestic Partnership/Cohabitating	168 (56.0%)	64 (64.0%)	53 (53.0%)	51 (51.0%)	
Single	61 (20.3%)	10 (10.0%)	23 (23.0%)	28 (28.0%)	
Divorced/Separated	52 (17.3%)	18 (18.0%)	16 (16.0%)	18 (18.0%)	
Widowed	19 (6.3%)	8 (8.0%)	8 (8.0%)	3 (3.0%)	
Other	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Education, n (%)					.0082
Elementary/primary school	2 (0.7%)	1 (1.0%)	1 (1.0%)	0 (0.0%)	
Secondary/high school	62 (20.7%)	15 (15.0%)	15 (15.0%)	32 (32.0%)	
Some college	95 (31.7%)	25 (25.0%)	35 (35.0%)	35 (35.0%)	
College degree	93 (31.0%)	39 (39.0%)	32 (32.0%)	22 (22.0%)	
Postgraduate degree	46 (15.3%)	20 (20.0%)	15 (15.0%)	11 (11.0%)	
Other[2]	2 (0.7%)	0 (0.0%)	2 (2.0%)	0 (0.0%)	
Employment status, n (%)					.0013
Full-time work	129 (43.0%)	54 (54.0%)	33 (33.0%)	42 (42.0%)	
Part-time work	32 (10.7%)	10 (10.0%)	11 (11.0%)	11 (11.0%)	
Student	2 (0.7%)	0 (0.0%)	2 (2.0%)	0 (0.0%)	
Unemployed	19 (6.3%)	3 (3.0%)	9 (9.0%)	7 (7.0%)	
Homemaker/stay-at-home parent	20 (6.7%)	4 (4.0%)	4 (4.0%)	12 (12.0%)	
Retired	36 (12.0%)	18 (18.0%)	10 (10.0%)	8 (8.0%)	
Disabled	60 (20.0%)	11 (11.0%)	29 (29.0%)	20 (20.0%)	
Other[3]	2 (0.7%)	0 (0.0%)	2 (2.0%)	0 (0.0%)	
Type of health insurance, n (%)[5]					
Private health plan	132 (44.0%)	50 (50.0%)	41 (41.0%)	41 (41.0%)	
Medicare/Medicaid	145 (48.3%)	54 (54.0%)	46 (46.0%)	45 (45.0%)	
Tricare/VA	13 (4.3%)	4 (4.0%)	8 (8.0%)	1 (1.0%)	
State-sponsored plan	17 (5.7%)	4 (4.0%)	8 (8.0%)	5 (5.0%)	
Other[4]	2 (0.7%)	0 (0.0%)	1 (1.0%)	1 (1.0%)	
No coverage	15 (5.0%)	3 (3.0%)	2 (2.0%)	10 (10.0%)	
No coverage	15 (5.0%)	3 (3.0%)	2 (2.0%)	10 (10.0%)	

SD, standard deviation.
[1] Other race include: White and American Indian or Alaska Native (n = 6), White and Black (n = 1), White and Asian or Asian American (n = 1), Hispanic (n = 1), and Mexican American (n = 1).
[2] Other education include: Medical Massage School after college (n = 1), Medical Assistant training (n = 1).
[3] Other employment include: Self-employed (n = 2).
[4] Other insurance include: Medical (n = 1), Security (n = 1).
[5] Not mutually exclusive.
[6] P-values reflect chi-square test for categorical data, and one-way ANOVA for continuous data (GLM model: treatment groups as independent and continuous variables as dependent).

Table 2. Participant clinical characteristics by treatment group.

		Treatment Group			
	Total (N = 300)	Mirabegron (N = 100)	Antimuscarinics (N = 100)	Untreated (N = 100)	P-Value[2]
Ever diagnosed with OAB, n (%)					< .0001
Yes	265 (88.3%)	99 (99.0%)	96 (96.0%)	70 (70.0%)	
No	35 (11.7%)	1 (1.0%)	4 (4.0%)	30 (30.0%)	
Years since OAB diagnosis, n (%)	n = 265	n = 99	n = 96	n = 70	.0460
Less than a year ago	41 (15.5%)	13 (13.1%)	13 (13.5%)	15 (21.4%)	
1-2 years ago	71 (26.8%)	25 (25.3%)	34 (35.4%)	12 (17.1%)	
3-5 years ago	73 (27.5%)	34 (34.3%)	24 (25.0%)	15 (21.4%)	
6-10 years ago	37 (14.0%)	14 (14.1%)	14 (14.6%)	9 (12.9%)	
More than 10 years ago	40 (15.1%)	12 (12.1%)	11 (11.5%)	17 (24.3%)	
Don't know	3 (1.1%)	1 (1.0%)	0 (0.0%)	2 (2.9%)	
Years since first OAB symptoms, n (%)					.0038
Less than a year ago	14 (4.7%)	2 (2.0%)	5 (5.0%)	7 (7.0%)	
1-2 years ago	71 (23.7%)	27 (27.0%)	23 (23.0%)	21 (21.0%)	
3-5 years ago	93 (31.0%)	32 (32.0%)	34 (34.0%)	27 (27.0%)	
6-10 years ago	53 (17.7%)	22 (22.0%)	21 (21.0%)	10 (10.0%)	
More than 10 years ago	63 (21.0%)	17 (17.0%)	17 (17.0%)	29 (29.0%)	
Don't know	6 (2.0%)	0 (0.0%)	0 (0.0%)	6 (6.0%)	
Comorbidities, n (%)[1]					
Diabetes	43 (14.3%)	17 (17.0%)	14 (14.0%)	12 (12.0%)	.5970
Interstitial cystitis	48 (16.0%)	29 (29.0%)	10 (10.0%)	9 (9.0%)	< .0001
Malignant disease of the pelvic organs	6 (2.0%)	1 (1.0%)	2 (2.0%)	3 (3.0%)	.6004
Kidney disease	9 (3.0%)	2 (2.0%)	5 (5.0%)	2 (2.0%)	.3567
Multiple sclerosis	8 (2.7%)	2 (2.0%)	4 (4.0%)	2 (2.0%)	.5983
Parkinson's disease	2 (0.7%)	2 (2.0%)	0 (0.0%)	0 (0.0%)	.1335
BPH	18 (6.0%)	6 (6.0%)	7 (7.0%)	5 (5.0%)	.1850
Stroke	19 (6.3%)	7 (7.0%)	8 (8.0%)	4 (4.0%)	.4817
Spina bifida	3 (1.0%)	3 (3.0%)	0 (0.0%)	0 (0.0%)	.0483
Spinal cord injury that affects bladder function	26 (8.7%)	20 (20.0%)	6 (6.0%)	0 (0.0%)	< .0001
Traumatic brain injury	6 (2.0%)	2 (2.0%)	2 (2.0%)	2 (2.0%)	1.0000
Current behavioral OAB treatments, n (%)[1]					–
Pelvic floor muscle exercises (Kegel)	100 (33.3%)	41 (41.0%)	33 (33.0%)	26 (26.0%)	–
Pelvic floor physical therapist	25 (8.3%)	24 (24.0%)	1 (1.0%)	0 (0.0%)	–
Scheduled/frequent urination	68 (22.7%)	31 (31.0%)	17 (17.0%)	20 (20.0%)	–
Limiting fluid intake	118 (39.3%)	46 (46.0%)	39 (39.0%)	33 (33.0%)	–
Losing weight	58 (19.3%)	10 (10.0%)	25 (25.0%)	23 (23.0%)	–
Bladder training	50 (16.7%)	20 (20.0%)	12 (12.0%)	18 (18.0%)	–
None of the above	125 (41.7%)	37 (37.0%)	42 (42.0%)	46 (46.0%)	–
Other[3]	3 (1.0%)	0 (0.0%)	1 (1.0%)	2 (2.0%)	–
Current pharmacologic OAB treatments, n (%)[1]	n = 200	n = 100	n = 100		–
Mirabegron	100 (50.0%)	100 (100%)	0 (0.0%)	N/A	–
Solifenacin	6 (3.0%)	0 (0.0%)	6 (6.0%)	N/A	–
Tolterodine	5 (2.5%)	0 (0.0%)	5 (5.0%)	N/A	–
Oxybutynin	72 (36.0%)	0 (0.0%)	72 (72.0%)	N/A	–
Fesoterodine	4 (2.0%)	0 (0.0%)	4 (4.0%)	N/A	–
Darifenacin	6 (3.0%)	0 (0.0%)	6 (6.0%)	N/A	–
Trospium	7 (3.5%)	0 (0.0%)	7 (7.0%)	N/A	–
Other[4]	1 (0.5%)	0 (0.0%)	1 (1.0%)	N/A	–
Duration on current OAB medication, n (%)[5]	n = 200	n = 100	n = 100		–
1-3 mo[6]	31 (15.5%)	15 (15.0%)	16 (16.0%)	N/A	–
4-6 mo	39 (19.5%)	27 (27.0%)	12 (12.0%)	N/A	–
7-12 mo	32 (16.0%)	16 (16.0%)	16 (16.0%)	N/A	–
More than 12 mo	98 (49.0%)	42 (42.0%)	56 (56.0%)	N/A	–
Current sleep aid treatments, n (%)[1]					–
Herbal supplement	96 (32.0%)	38 (38.0%)	33 (33.0%)	25 (25.0%)	–
Over-the-counter sleep aid	58 (19.3%)	22 (22.0%)	19 (19.0%)	17 (17.0%)	–
Prescription sleep aid	84 (28.0%)	31 (31.0%)	34 (34.0%)	19 (19.0%)	–
Taking sleep aid but don't know what type	6 (2.0%)	1 (1.0%)	2 (2.0%)	3 (3.0%)	–
Not taking any sleep aids	116 (38.7%)	33 (33.0%)	37 (37.0%)	46 (46.0%)	–
Don't know	2 (0.7%)	0 (0.0%)	0 (0.0%)	2 (2.0%)	–
Current depression medication, n (%)					–
Yes	123 (41.0%)	43 (43.0%)	52 (52.0%)	28 (28.0%)	–
No	176 (58.7%)	57 (57.0%)	48 (48.0%)	71 (71.0%)	–

Table 2 (Continued)

	Total (N = 300)	Treatment Group Mirabegron (N = 100)	Antimuscarinics (N = 100)	Untreated (N = 100)	P-Value[2]
Don't know	1 (0.3%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	–
Current BPH medication, n (%)[7]	n = 97	n = 38	n = 22	n = 37	–
Yes	23 (23.7%)	14 (36.8%)	6 (27.3%)	3 (8.1%)	–
No	73 (75.3%)	24 (63.2%)	16 (72.7%)	33 (89.2%)	–
Don't know	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (2.7%)	–
OAB-q SF domains					
Symptom bother	53.3 (24.8)	53.3 (24.9)	56.7 (23.7)	50.1 (25.6)	–
HRQoL	48.5 (26.4)	48.7 (27.2)	51.1 (25.2)	45.8 (26.9)	–

BPH, benign prostatic hyperplasia; HRQoL, health-related quality of life; OAB, overactive bladder.

[1] Percentages may not add up to 100% as more than one option can be selected.

[2] *P*-values reflect chi-square test for categorical data, and one-way ANOVA for continuous data (GLM model: treatment groups as independent and continuous variables as dependent).

[3] Other behavioral OAB treatments include: diet and frequent position change to avoid sitting too long (n = 1), incontinence products (n = 1), pullups and diapers (n = 1).

[4] Other pharmacologic OAB treatments include: Tamsulosin (n = 1). Note: two untreated participants reported with Tamsulosin (n = 1), AZO Bladder Supplements (n = 1).

[5] Untreated participants were not asked for this question.

[6] Participants taking current OAB medication for less than 1 month were disqualified.

[7] Only males were asked about current BPH medication.

Employment status also differed significantly among treatment groups, with 54.0% of mirabegron participants, 33.0% of antimuscarinics participants, and 42.0% of untreated participants reported having full-time work (*P*-value = .001).

Clinical characteristics for the sample and stratification by treatment group are presented in Table 2. Interstitial cystitis and diabetes were the most common comorbid conditions reported by participants (16.0% and 14.3%, respectively). A larger proportion of participants on mirabegron reported interstitial cystitis (29.0%) and/or spinal cord injury (20.0%) compared to antimuscarinic (10.0% and 6.0%, respectively) or untreated participants (9.0% and 0.0%, respectively) (*P*-value < .0001). Participants were classified as having OAB based on an OAB diagnosis (88.3%) or based on reported OAB symptoms (11.7%). The number of participants classified based on OAB diagnosis alone was lower among the untreated group (70.0%) compared to the mirabegron (99.0%) or antimuscarinics groups (96.0%) (*P*-value < .0001). A higher proportion of untreated participants reported onset >10 years ago (29.0%) compared to participants on mirabegron (17.0%) or antimuscarinics (17.0%) (*P*-value = .004). Among participants taking antimuscarinics, 72.0% were taking oxybutynin. 49% taking pharmacologic treatment reported taking their current medication for >12 months.

Mean (SD) OAB-q bother scores were 53.3 (SD 24.8) for the overall study sample, and 53.3 (24.9), 56.7 (23.7), and 50.1 (25.6) among the mirabegron, antimuscarinics, and untreated groups, respectively (Table 2). OAB-q HRQoL scores were 48.5 (26.4) for the overall study sample, and 48.7 (27.2), 51.1 (25.2), 45.8 (26.9) among the mirabegron, antimuscarinics, and untreated groups respectively.

Analysis of Potential Covariates

Among the six covariates initially considered for inclusion in ANCOVA, no significant differences were found by treatment group (Supplementary Table 1). Additional covariates were identified and included in the ANCOVA models, including ethnicity, diabetes, interstitial cystitis, sleep aid medication use, and depression medication use.

Differences in symptom severity by treatment group as measured by the LURN SI-10 total score were noted; however, the LURN SI-10 total score was highly correlated with OAB-q SF Symptom Bother score and was therefore not included as a covariate in the model to avoid collinearity.

Sleep Disturbance: PROMIS-29 Sleep Disturbance Subscale

The mean (SD) T-scores for sleep disturbance were 56.6 (7.3) for mirabegron participants, 58.2 (8.8) for antimuscarinic participants, and 57.6 (8.3) for untreated participants (lower values indicating less sleep disturbance; Table 3). There were no statistically significant differences among these groups (see ANCOVA results below for more details). The most frequently reported sleep problems were poor sleep quality and sleep not being refreshing, with 25% of the total sample indicating that their sleep was not at all refreshing (Supplementary Table 2). The proportion of participants who reported their sleep was not at all refreshing was lowest among mirabegron participants (18.0%; Supplementary Tables 3-5). Nearly half (46.7%) of all participants reported their sleep quality as poor or very poor; the proportion who reported their sleep quality as poor or very poor was lowest among mirabegron participants (39.0%). Further details regarding items on the PROMIS-29 Sleep

Table 3. Treatment group differences in sleep disturbance, depression, and nocturia.

| | Treatment Groups | | | | | Pairwise Comparison[2] Least Squares Mean Difference (SE), |
	Mirabegron (N = 100)	Antimuscarinics (N = 100)	Untreated (N = 100)	F	P-Value[1]	P-Value
Sleep Disturbance (PROMIS-29)				7.37	< .0001	1: − 1.0 (1.1), 1.0000; 2: − 1.6 (1.1), .4339; 3: − 0.6 (1.1), 1.0000
n	100	100	97			
Least Squares Mean (SE)	54.9 (1.0)	55.9 (1.2)	56.5 (1.2)			
Mean (SD)	56.6 (7.3)	58.2 (8.8)	57.6 (8.3)			
Median	55.6	58.1	58.0			
Min to Max	36.9-73.3	32.0-73.3	36.9-73.3			
Sleep Disturbance (PROMIS Sleep Disturbance Short Form 8b)				8.32	< .0001	1: − 1.2 (1.1), .9280; 2: − 2.0 (1.1), .2356; 3: − 0.9 (1.1), 1.0000
n	100	100	97			
Least Squares Mean (SE)	55.5 (1.1)	56.7 (1.2)	57.6 (1.2)			
Mean (SD)	57.7 (8.3)	59.5 (8.7)	59.2 (8.8)			
Median	57.4	59.8	58.6			
Min to Max	36.1-76.5	35.8-76.5	37.8-76.5			
Depression (PROMIS-29)				14.18	< .0001	1: − 0.3 (1.2), 1.0000; 2: − 2.2 (1.2), .2411; 3: − 1.8 (1.2), .4068
n	100	100	99			
Least Squares Mean (SE)	60.2 (1.2)	60.5 (1.3)	62.4 (1.3)			
Mean (SD)	58.0 (10.03)	59.1 (10.02)	58.8 (9.5)			
Median	58.9	61.9	59.6			
Min to Max	41.0-79.3	41.0-79.3	41.0-79.3			
Nocturia (LURN SI-10, item 10)				13.06	< .0001	1: − 0.0 (0.1), 1.0000; 2: − 0.1 (0.1), 1.0000; 3: − 0.0 (0.1), 1.0000
n	100	100	96			
Least Squares Mean (SE)	2.1 (0.1)	2.2 (0.1)	2.2 (0.1)			
Mean (SD)	2.1 (0.8)	2.0 (0.8)	2.0 (0.9)			
Median	2.0	2.0	2.0			
Min to Max	0.0-3.0	0.0-3.0	0.0-3.0			

SD, standard deviation; SE, standard error.
[1] From analysis of covariance model (ANCOVA): controlling OAB Bother Score, Age, Gender, Ethnicity, Diabetes, Interstitial Cystitis, Sleep Aid medication and Depression medication.
[2] Pairwise comparisons between LS means, Bonferroni correction for multiple comparisons: 1= Mirabegron Patients vs. Antimuscarinic patients; 2= Mirabegron Patients vs. untreated patients; 3= Antimuscarinic patients vs. untreated patients.

Disturbance Subscale are reported in Supplementary Tables 2-5.

Depression: PROMIS-29 Depression Subscale

The mean (SD) PROMIS-29 depression domain T-scores were 58.0 (10.03) among mirabegron participants, 59.1 (10.02) among antimuscarinic participants, and 58.8 (9.5) among untreated participants (lower scores indicating less depression; Table 3). Among the total sample, 30.7% reported that they felt depressed often or always (Supplementary Table 2); similarly, 30% of the mirabegron group, 33% of the antimuscarinic group, and 29% of the untreated group reported that they felt depressed often or always (Supplementary Tables 3-5). Item details for the PROMIS-29 Depression Subscale are reported in Supplementary Tables 2-5.

Sleep Disturbance: PROMIS Sleep Disturbance Short Form 8B

The mean (SD) T-score from the PROMIS Sleep Disturbance Short Form 8b was 57.7 (8.3) among mirabegron participants, 59.5 (8.7) among antimuscarinic participants, and 59.2 (8.8) among untreated participants (lower values indicating less sleep disturbance; Table 3). The most common problems reported on the PROMIS Sleep Disturbance Short Form 8b included poor satisfaction with sleep and not getting enough sleep: 39.3% indicated they were not at all satisfied with their sleep; 59.6% indicated that they rarely or never get enough sleep (Supplementary Table 2). Mirabegron participants comprised the smallest proportion of those who gave these responses. Further details regarding items on the PROMIS Sleep Disturbance Short Form 8b are reported in Supplementary Tables 2-5.

Nocturia: LURN Symptom Index-10

Regarding nocturia (as measured by the LURN SI-10), 94.4% of all study participants reported waking up ≥1 time to urinate during a typical night in the past 7 days, while 77.7% reported waking up ≥2 times (Supplementary Table 6). The frequency of nocturia was similar between treatment groups: 96.0%, 96.0%, and 91.0% of mirabegron, antimuscarinic, and untreated participants, respectively, reported waking up to ≥1 time to urinate (Supplementary Tables 7-9). Additionally, 80.0%, 79.0%, and 74.0% of mirabegron, antimuscarinic, and untreated participants, respectively, reported waking up to urinate ≥2 times. Further details regarding items on the LURN SI-10 are reported in Supplementary Tables 6-9.

ANCOVA Results: Sleep Disturbance, Depression, and Nocturia

For all study outcomes (PROMIS-29 Sleep Disturbance Subscale, PROMIS-29 Depression Subscale, PROMIS Sleep Disturbance Short Form 8B, and LURN Symptom Index-10), the overall F values for all ANCOVA models for group differences were statistically significant (all P-values < .0001; Table 3). However, follow-up Bonferroni-adjusted pairwise tests found no significant differences in the least squares mean values for any of the outcomes between treatment groups.

Sensitivity Analyses

Sensitivity analyses were conducted to compare the FAS to the per protocol set (PPS), which contained participants who met all eligibility criteria only by excluding the 52 individuals with a protocol violation. All analyses and treatment group comparisons conducted in the FAS were replicated in the PPS and were observed to produce similar results with no apparent effect on study conclusions. Thus, only the results from the FAS have been presented in this manuscript.

To further investigate the potential impact of patients with spinal cord injury in this cohort, the authors reviewed the mean scores among seven individuals with spinal cord injury from the PPS for the PROMIS-29 Sleep Disturbance Subscale and the PROMIS Sleep Disturbance Short Form 8B. The mean score among the individuals with spinal cord injury for the PROMIS-29 Sleep Disturbance Subscale (60.7 [SD 9.42]) fell within a reasonable range of the mean score among the FAS (57.5 [SD 8.6]; t-test P-value > .05). Similarly, for the PROMIS Sleep Disturbance Short Form 8B, the mean score (61.9 [SD 8.76]) was reasonably within the range of the mean score among the FAS (58.8 [SD 8.6]; t-test P-value > .05). As a result, we believe that excluding patients with spinal cord injury would not affect the study conclusion and therefore were retained in the FAS.

DISCUSSION

This study is the first to compare sleep disturbance among adults with OAB by treatment. Across all treatment groups, all outcomes were consistently bothersome. The mirabegron group trended lowest of the three treatment groups across all outcomes studied, though no significant group differences were found. Regardless of treatment use, participants with OAB faced more severe sleep disturbance symptoms than the general population as observed in the elevation by up to one SD of all PROMIS-29 domain scores in all three treatment groups above the US general population scores. Nocturia was notably common and reported by over three-quarters of the study population despite most participants using mirabegron or an antimuscarinic.

This study's findings are aligned with others showing higher sleep disturbance and fatigue among OAB patients than non-OAB, as a result of nocturia.[8] Intensity of OAB symptoms, particularly urge incontinence and nocturia, have been found to drive depression and anxiety.[18]

There are limitations to this study inherent to the cross-sectional design. Causal relationships and longitudinal changes in participant responses following the initiation of pharmacological treatments could not be evaluated. Next, OAB status was determined by self-report and not otherwise verified. However, surveys of self-identified patients are common; associated limitations are documented.[19-21] Further research could replicate findings among patients with confirmed diagnoses. This sample may have been subject to survival bias, overrepresenting participants with longer duration of OAB. Since treatment groups were non-randomized, associations between outcomes and baseline characteristics may be subject to confounding by unmeasured characteristics; however, some were controlled for in the ANCOVA models. The inclusion of participants with interstitial cystitis in the sample affected the mean age of participants and LURN SI-10 total scores, although this was controlled for in the analyses and assessed during the sensitivity analysis.

CONCLUSION

In this study, adults with OAB experienced worse sleep disturbance and depression relative to the US general population regardless of treatment type; nocturia was also particularly bothersome. Patients using mirabegron had consistently, though not statistically significantly, lower scores than the other two treatment groups across sleep-related outcomes. Future studies should examine changes in symptoms over time to assess temporal associations between treatment, sleep disturbance, and related outcomes.

Data Sharing Statement

Researchers may request access to anonymized participant-level data, trial-level data, and protocols from Astellas sponsored clinical trials at www.clinicalstudydatarequest.com. For the Astellas criteria on data sharing see: https://clinicalstudydatarequest.com/Study-Sponsors/Study-Sponsors-Astellas.aspx.

Declaration of Competing Interest

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.urology. 2023.06.014.

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