



## Predictors of Variability in Urinary Incontinence and Overactive Bladder Symptoms

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**Aims:** We used data from the General Longitudinal Overactive Bladder Evaluation (*GLOBE*) to understand predictors of variation in urgency and urinary incontinence (UI) symptoms over time. **Methods:** A random sample of Geisinger Clinic primary care patients (men and women) 40+ years of age were recruited for a survey of bladder control symptoms at baseline and 12 months later. Symptom questions used a 4-week recall period. Composite scores were derived for urgency and UI frequency. Logistic regression was used to evaluate predictors of variation in scores at cross-section and longitudinally. **Results:** A majority of those with UI symptoms and almost 40% of those with urgency symptoms reported episodes of once a week or less often; 17% had symptoms a few times a week or more often. Twenty-one percent with urgency symptoms and 25% with UI symptoms at baseline did not have active symptoms 12 months later. The strongest predictors of active symptoms at follow-up were baseline symptom score and duration of time since first onset of symptoms. Of those with no urgency symptoms at baseline, 22% had urgency at 12 months. Among those with no UI symptoms at baseline, 13% had UI symptoms 12 months later. Among the latter, age (males only) and BMI were the strongest predictors of symptoms at follow-up. **Conclusions:** Inter-individual and intra-individual occurrences of urgency and UI symptoms are highly variable in the general population. Use of established predictors to select individuals with less variability in symptoms may help to reduce placebo rates in clinical trials. *NeuroUrol. Urodynam.* 29:328–335, 2010. © 2009 Wiley-Liss, Inc.

**Key words:** epidemiology; incontinence; longitudinal; urgency

### INTRODUCTION

Bladder control symptoms of urgency and urinary incontinence (UI) is highly prevalent among both men and women, rapidly increases in prevalence after age 40, and is strongly associated with poorer quality of life and higher prevalence of depression.<sup>1–10</sup> This pattern is common to many symptomatic conditions that impair function. Notably, the occurrence of bladder control symptoms has epidemiologic features similar to many chronic episodic conditions (e.g., migraine,<sup>11</sup> mood disorders,<sup>12</sup> asthma,<sup>13</sup> gastro-esophageal reflux disease,<sup>14</sup> and others. There is substantial variation in inter-individual symptom occurrence. For example, individuals can vary in their migraine headache attack rate from 1 per year to daily headaches.<sup>15</sup> There is also substantial intra-individual variation. For example, individuals can suffer from frequent migraine headaches during one time period, followed by a period where attacks are substantially less frequent.<sup>16</sup> In addition, individuals can progress to more severe symptom states, characterized by more frequent and severe symptoms, and regress to a less severe state, reflecting a highly fluid process for these types of conditions.<sup>16</sup> A relatively small proportion of those with chronic episodic disorders suffer from frequent symptoms (e.g., symptoms every other day to every day), and an even smaller proportion suffer from frequent symptoms that persist over long periods of time.<sup>14,16</sup>

While bladder control problems (i.e., overactive bladder, stress, urge, and mixed UI) are often described as chronic

persistent disorders, epidemiologic data indicate substantial variation in symptom expression among individuals at a given point and within individuals over time.<sup>17</sup> The epidemiology of bladder control disorders has many parallels to the common chronic episodic disorders. We believe these parallels have implications for placebo response rates in clinical trial treatments for bladder control and for approaches to treatment (e.g., use of preventive vs. acute rescue medications).

The purpose of this study is to describe inter- and intra-individual variation in incontinence and overactive bladder symptoms using data from the General Longitudinal

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Overactive Bladder Evaluation (*GLOBE*) and to identify factors associated with variation.

**METHODS**

In the *GLOBE* study, Geisinger Clinic primary care patients at least 40 years of age completed a questionnaire on bladder control at baseline and 12 months later. In this section, we briefly summarize details on the Bladder Health Survey (BHS), the source population for the study sample, the sampling and survey methods. The study was approved by the Geisinger Institutional Review Board.

**Questionnaire**

The BHS is a self-administered mailed questionnaire and includes questions on the occurrence (i.e., never or rarely, a few times, about once a week, a few times a week, every day) of urgency, frequency, nocturia, and urine loss in the previous 4 weeks. For those reporting UI symptoms, specific questions are asked about stress UI symptoms and urge UI symptoms. Most of the BHS items were derived from previously validated questionnaires.<sup>6,10,18,19</sup> In particular, questions relevant to overactive bladder, urgency, and urge incontinence were largely derived from the NOBLE study.<sup>10</sup> Other questions specific to incontinence subtype were taken from Herzog et al.<sup>18</sup>

A test–retest reliability study of the BHS was completed in a random sample of 161 Geisinger Clinic primary care patients, age 45–75, with a clinical encounter in the last 2 years (Table I). The age criterion was expanded to 40 years and older for the longitudinal study. Participants in the reliability study completed the same questionnaire twice with an approximately 2-week interval between mailings. With one exception, reliability (i.e., Spearman’s correlation coefficient) of UI-related items (Table II) ranged from 0.71 to 0.83. Reliability of composite scores (see Table II) ranged from 0.77 to 0.86.

**Definition of Urgency and UI**

Symptom measures were based on multiple questions as a means to improve reliability. The urgency measure was based on responses to four questions (Table II, questions 2–5), had a range of 0–12, and had a test–retest reliability of 0.86. For purposes of analysis, we defined an individual as having active urgency symptoms in the previous 4 weeks if their overall score was 3+, indicating that they reported a couple of urgency episodes or more on three to four questions. The UI symptom measure was based on two questions (Table II, questions 16 and 17), had a score range of 0–6, and had a test–retest reliability of 0.85. For purposes of analysis, we

defined an individual as having active UI symptoms if their score was 2+, indicating that they reported a couple of UI episodes or more on the two UI questions.

**Source Population, Sample Selection, and Data Collection**

Men and women for this study were randomly selected from primary care patients in the Geisinger Clinic, part of the Geisinger Health System (GHS), an integrated health-care system that serves residents in 31 of 67 counties in central and northeastern Pennsylvania. The Geisinger Clinic includes 40 Community Practice sites that provide primary care to more than 400,000 patients. Primary care patients were eligible for selection if they had a clinical encounter within the past 4 years and were at least 40 years of age. At baseline, 15,682 patients were randomly selected for participation. Seven to 10 days after receiving a pre-notification letter, individuals were sent the BHS. The survey was accompanied by an introductory cover letter and a \$2 bill.<sup>20</sup> A reminder letter was mailed to non-respondents 2 weeks later. The overall response rate to the baseline survey was 44% (n = 6,937).

A follow-up questionnaire was sent 12 months after the baseline survey. As in the baseline survey, a \$2 bill was included with the survey and a reminder letter was mailed to non-respondents after 2 weeks. All individuals who met the threshold criteria for the presence of urgency symptoms of 3+ and/or UI symptoms of 2+ at baseline, as well as a randomly selected subset of individuals who did not meet the criteria, were sent a survey. The response rate to the 12-month survey was 71%.

**Analysis**

We first describe variation in symptom scores at baseline among those reporting urgency (i.e., urgency score of 3+) or UI (i.e., UI score of 2+) symptoms, followed by analysis of change in symptom scores between baseline and follow-up. Logistic regression was used to model the relation between active urgency (i.e., urgency score of 3+) or UI symptom status (i.e., UI score of 2+) at baseline and the odds of exhibiting active symptoms at follow-up. SAS version 9.1 was used for all analysis (SAS Institute, Inc., Cary, NC). Urgency and UI status were categorically defined as dependent variables. The odds of having active symptoms at follow-up were modeled in relation to baseline symptom status (i.e., defined as a continuous variable), age (40–49, 50–59, 60–69, 70+), marital status (married, widowed, divorced/separated, never married), education (11 years or less, high school grad/GED, some college or tech school, college graduate, any post-graduate work), urinary tract infection (UTI) status (Yes/No) in the previous 4 weeks, parity (0, 1, 2, 3+), body mass index

TABLE I. Characteristics of Reliability, Baseline Only, and Baseline/12-Month Samples

Variable	Category	Reliability sample (n = 161)		Baseline only sample (n = 3,033)		Baseline/12-month sample (n = 3,823)		P-value
		n	%	n	%	n	%	
Age <sup>a</sup>	40–49	30	19	1,154	38	765	20	<0.0001
	50–59	58	36	933	31	1,049	27	
	60–69	50	31	491	16	804	21	
	70+	23	14	455	15	1,205	32	
Gender	Male	61	38	1,586	52	1,671	44	<0.0001
	Female	100	62	1,447	48	2,152	56	

<sup>a</sup>Reliability sample was limited to individuals age 45–75. Longitudinal sample was expanded to 40+ years.

TABLE II. Test–Retest Reliability (i.e., 2 Weeks Between Questionnaires) of UI-Related Question Responses and Composite Scores From the Bladder Health Survey (n = 162)

Question domain	Q#	Response format	Question	Test–retest reliability Spearman's r	
				Item	Composite score
Urgency	2	How often in past 4 weeks <sup>a</sup>	Suddenly have a feeling that your bladder was full	0.80	0.86
	3		Have a sudden an uncomfortable feeling that you had to urinate soon	0.76	
	4		Have such a strong urge to urinate that you had to stop what you were doing and rush to the bathroom	0.83	
	5		Have very little warning before you were about to lose urine beyond your control	0.80	
	16		Lose any urine, even a small amount?	0.83	
Urine loss and amount of loss	17	Lose more than a few drops or small amount of urine?	0.73		
	19	How much urine do you leak each time? <sup>c</sup>	0.63	N/A	
	26	Were coughing hard, laughing, or sneezing?	0.74	0.77	
Stress incontinence	27	How often did you lose urine because you? <sup>b</sup>	Were lifting, pushing, or pulling a heavy object?	0.71	
	23	Had trouble getting to the bathroom in time?	0.72	0.79	
Urge incontinence	24	Had a sudden urge to urinate?	0.73		

<sup>a</sup>Response option: never or rarely (0), a few times (1), about once a week (2), a few times a week (2), every day (3).

<sup>b</sup>Response option: never or rarely (0), less than half the time (1), half the time or more (2), always (3).

<sup>c</sup>Response option drops or little small amounts more than a small amount.

(BMI based on self-reported height and weight and categorized as <25, 25–29.99, 30+), and duration of time since onset of symptoms. The latter was self-reported in response to the question, “For how many months or years have you had urine loss (or “... a sudden urge to urinate”)?”

Logistic regression was used to model the relation between inactive urgency (i.e., urgency <3) or UI symptom status (i.e., UI score <2) at baseline and the odds of reporting active symptoms at 12 months. Urgency and UI status were categorically defined as dependent variables. The same covariates described above were used in these models, with the exception of the baseline score and duration since onset of symptoms, which were excluded as respondents reporting no symptoms at baseline were instructed to skip the duration questions.

## RESULTS

More than half of those reporting urgency or UI symptoms at baseline were 60+ years of age; a majority were married, and 45–49% had some college education (Table III). Approximately 40% had a BMI of 30+. Among females, 11% were nulliparous and 42% had three or more births. On average, duration of time with urgency or UI symptoms was shorter for males than for females. Moreover, the distribution of duration times for urgency was considerably shorter than the times for UI. A total of 101 individuals with a baseline UI score of 2+ and 770 individuals with a baseline urgency score of 3+, did not report a duration value. Individuals missing urgency duration responses were more likely to be younger, male, and have a lower BMI than those with duration responses. Individuals who did not report a duration value for urine loss were more likely to be male, older, have a lower BMI, be a widower, and be less educated than individuals with urine loss duration responses.

### Cross-Sectional Analysis

Individuals without urgency or UI symptoms at baseline (Table III) were younger, more likely to be a college graduate,

have a lower BMI, and fewer births (i.e., women only) than their counterparts with active symptoms, differences explained, in part, by age and cohort effects. Among those with a baseline urgency score of 3+ (males = 1,383, females = 1,880), approximately 41% of males and 36% of females had a baseline urgency score of 3 or 4 (i.e., episodes occurred a few times a month to once a week) and 15% of males and 26% of females had a score of 9–12 (i.e., episodes occurred a few times a week to every day). Among those with a baseline UI score of 2+ (males = 683, females = 1,566), 67% of males and 56% of females had baseline UI scores of 2 or 3 (i.e., UI episodes occurred a few times a month to once a week) and approximately 21% of males and females had a UI score of 5–6 (i.e., UI episodes a few times a week to every day).

The mean urgency score of 5.8 (SE = 0.07) for males was significantly lower than the mean score of 6.5 for females (SE = 0.07;  $P < 0.0001$ ). Unadjusted scores varied modestly by age for both males and females, but substantial variation was observed by education (i.e., less than a high school education vs. other levels), UTI in the previous 4 weeks, BMI (females only), and duration of time with urgency (Table III). For the latter, the 30.3% of males and 18.7% of females who did not report duration of time with urgency (i.e., denoted “missing” in Table III), had mean urgency scores of 4.5 and 4.7 for males and females, respectively. The mean urgency score for those who reported that symptoms started within the past 6 months was similar to the mean score of those who were missing duration data. In contrast, the mean urgency scores were substantially higher among all subgroups who reported that their duration of time since onset was 6 months or more.

The mean UI symptom score varied significantly by education (i.e., less than a high school education vs. higher levels of education), BMI (females only), UTI in the past 4 weeks, and reported duration of time with UI. A relatively small percentage of those with elevated UI scores of 2+ did not report duration of time with UI (i.e., 5.9% of males, 3.9% of females). The mean UI scores for those missing duration data were similar to the mean UI score among those reporting that UI started in the previous 6 months. In contrast, the mean UI

TABLE III. Percent Distribution of Male and Female Characteristics at Baseline, GLOBE Study 2008

Variable	No symptoms at baseline <sup>a</sup>						Active symptoms at baseline <sup>b</sup>					
	Males			Females			Males			Females		
	Urgency	UI	%	Urgency	UI	%	Urgency	UI	%	Urgency	UI	%
Age	(n = 1,854)	(n = 2,550)	(n = 1,677)	(n = 1,979)	(n = 1,383)	(n = 683)	Mean baseline score (SE)	% (n = 1,880)	Mean baseline score (SE)	% (n = 1,566)	Mean baseline score (SE)	
40-49	33	30	32	32	19	16	5.4 (0.1)	27	6.3 (0.1)	26	3.3 (0.1)	
50-59	32	32	30	29	27	25	5.6 (0.1)	26	6.4 (0.1)	27	3.5 (0.1)	
60-69	19	20	17	17	22	21	5.7 (0.1)	18	6.6 (0.2)	17	3.5 (0.1)	
70+	15	18	21	22	31	38	6.2 (0.1)	30	6.6 (0.1)	30	3.5 (0.1)	
Marital status	6	6	5	5	5	5	6.0 (0.3)	5	6.6 (0.3)	5	3.5 (0.2)	
Never married	80	80	70	69	78	77	5.7 (0.1)	63	6.4 (0.1)	64	3.4 (0.1)	
Married	11	11	12	12	10	10	5.8 (0.2)	13	6.8 (0.2)	13	3.4 (0.1)	
Divorced/sep	3	4	13	14	7	8	6.0 (0.3)	19	6.5 (0.2)	19	3.6 (0.1)	
Widowed	7	7	9	9	10	11	6.2 (0.3)	11	7.1 (0.2)	12	3.6 (0.1)	
Education	37	37	40	41	39	40	5.7 (0.1)	45	6.4 (0.1)	45	3.4 (0.1)	
<HS Diploma	26	26	24	23	26	28	5.7 (0.1)	23	6.6 (0.1)	24	3.5 (0.1)	
HS Dip/GED	31	29	27	27	24	21	5.6 (0.1)	20	6.2 (0.1)	20	3.3 (0.1)	
Some college	22	21	39	38	18	18	5.6 (0.2)	27	5.9 (0.1)	25	3.2 (0.1)	
College grad+	47	46	33	34	43	44	5.7 (0.1)	34	6.5 (0.1)	33	3.4 (0.1)	
Body mass index	31	33	28	28	39	39	5.9 (0.1)	40	6.8 (0.1)	43	3.6 (0.1)	
<25	99	99	98	97	97	95	5.7 (0.1)	94	6.4 (0.1)	95	3.4 (0.0)	
25-29.99	1	1	2	3	4	5	7.1 (0.5)	6	7.0 (0.3)	5	4.1 (0.2)	
30+	16	15	16	15	10	12	5.9 (0.2)	12	5.9 (0.2)	12	3.3 (0.1)	
UTI past 4 weeks	1	1	16	14	12	12	6.4 (0.2)	12	6.4 (0.2)	13	3.4 (0.1)	
No	35	35	35	35	17	25	6.3 (0.2)	21	7.0 (0.1)	25	3.3 (0.1)	
Yes	33	33	33	36	18	25	7.0 (0.2)	19	7.5 (0.2)	26	3.6 (0.1)	
Parity	1	1	2	3	12	19	7.0 (0.2)	15	8.0 (0.2)	24	4.0 (0.1)	
0	1	1	2	3	4	5	5.8 (0.1)	4	4.7 (0.1)	4	2.8 (0.2)	
1	16	15	16	14	10	11	4.8 (0.2)	13	5.0 (0.1)	10	2.5 (0.1)	
2	35	35	35	35	12	15	5.9 (0.2)	13	6.3 (0.2)	12	3.2 (0.1)	
3+	33	33	33	36	17	25	6.3 (0.2)	21	7.0 (0.1)	25	3.3 (0.1)	
Duration since onset of symptoms	33	33	33	36	18	25	7.0 (0.2)	19	7.5 (0.2)	26	3.6 (0.1)	
Missing	33	33	33	36	12	19	7.0 (0.2)	15	8.0 (0.2)	24	4.0 (0.1)	
<6 months	33	33	33	36	12	19	7.0 (0.2)	15	8.0 (0.2)	24	4.0 (0.1)	
6-12 months	33	33	33	36	12	19	7.0 (0.2)	15	8.0 (0.2)	24	4.0 (0.1)	
1-2 years	33	33	33	36	12	19	7.0 (0.2)	15	8.0 (0.2)	24	4.0 (0.1)	
3-5 years	33	33	33	36	12	19	7.0 (0.2)	15	8.0 (0.2)	24	4.0 (0.1)	
>5 years	33	33	33	36	12	19	7.0 (0.2)	15	8.0 (0.2)	24	4.0 (0.1)	
Total	33	33	33	36	12	19	5.8 (0.1)	15	6.5 (0.1)	24	3.4 (0.0)	

<sup>a</sup>No urgency symptoms = urgency symptoms score <3. No UI symptoms = UI score <2.

<sup>b</sup>Active urgency = urgency symptoms score >3. Active UI = UI symptom score ≥2.

scores increased among those who reported time since onset of 6 months or more, especially for females.

**Longitudinal Analysis**

When evaluating change in symptom scores (i.e., baseline score minus follow-up score) among individuals with active symptoms at baseline, it is important to recognize that all individuals included in this analysis had an urgency of 3+ and/or a UI score of 2+ at baseline. The urgency score ranged from 3 to 12 at baseline, but could vary from 0 to 12 at 12 months. Similarly, the UI score ranged from 2 to 6 at baseline, but could vary from 0 to 6 at follow-up. The lower floor (i.e., score = 0) for scores at follow-up will result in a tendency for scores to improve with time. Figure 1a shows substantial changes in the urgency score (baseline minus 12-month follow-up) among those who had active urgency symptoms at baseline. For most individuals, the urgency score remained the same or improved (i.e., a positive score indicates that the symptom score declined between baseline and follow-up). The overall mean urgency score change was 0.88 (SE = 0.09) for males and 0.69 (SE = 0.08) for females (data not shown in Table III). Figure 1b shows a similar pattern for the UI severity score, where the score improved among more than half of those reporting UI symptoms at baseline. The overall mean change in the UI severity score was 0.65 for males (SE = 0.08) and 0.55 (SE = 0.50) for females.

Logistic regression was used to estimate the odds of reporting active symptoms (i.e., urgency score of 3+, UI symptom score of 2+) at 12 months, given active symptoms

at baseline (Table IV). Reporting active urgency symptoms at 12 months was strongly associated with baseline urgency score (i.e., increase odds of 0.35 per unit increase in score) and duration of time since onset of symptoms. Active symptom status was also associated with older age and lower education (Table IV). For age among females, the highest odds ratio was observed for those 60–69 years of age compared to those who were 40–49, while among males the highest odds ratio for age was observed for those 70 and older. Compared to those who were missing a duration value, the odds ratios for having active urgency symptoms at follow-up were substantially higher than 1.0 for all groups that had urgency symptoms for 6 months or more (Table IV). The odds ratio for reporting active UI symptoms at 12 months was also strongly associated with baseline score and with duration of time since onset of symptoms. In addition, active UI symptom status was associated with lower education in women (i.e., higher odds for those with <HS diploma), higher BMI, older age, and parous compared to nulliparous women. Compared to those who were missing a duration value, the odds ratios for having active UI symptoms at follow-up were substantially higher than 1.0 for all groups, but particularly for both males and females reporting that they had UI symptoms for more than 6 months (Table IV).

Of those with no urgency symptoms at baseline, 22% had urgency 12 months later and among those with no UI symptoms at baseline, 13% had UI symptoms at 12 months. Among those with active symptoms at 12 months, the mean urgency score was 4.31 (SD 1.79) and the mean UI score was 2.56 (SD 0.97).

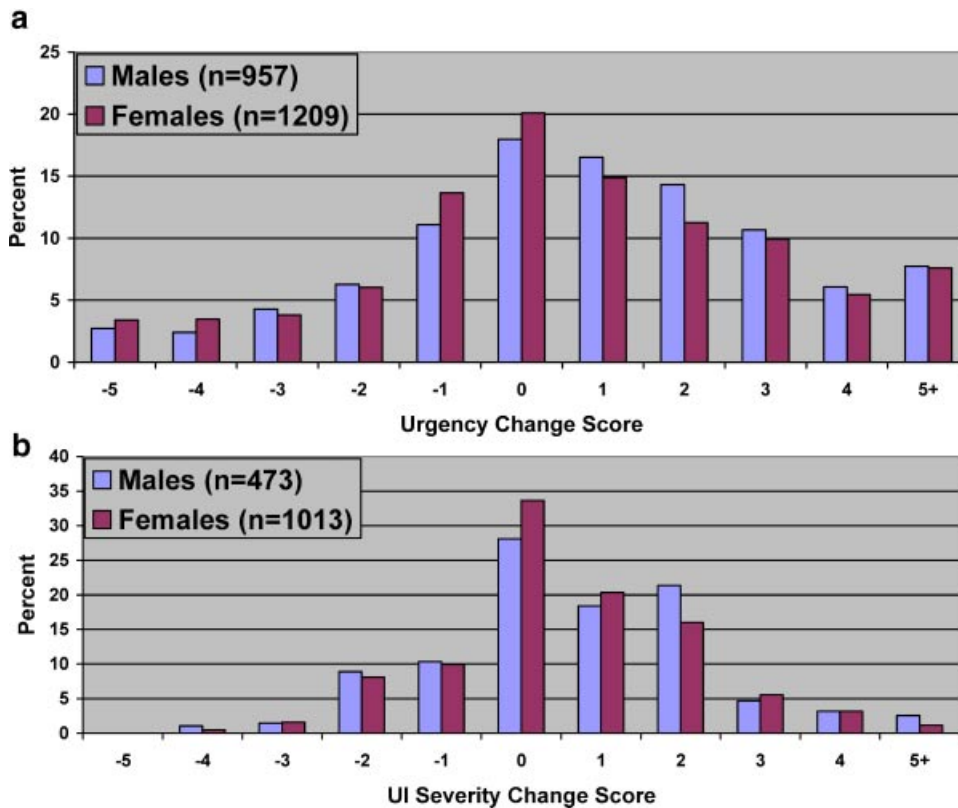


Fig. 1. Percent distribution of males and females by (a) urgency change score among individuals with active symptoms (urgency 3+) at baseline and (b) UI severity change score among individuals with active symptoms (UI 2+) at baseline.

TABLE IV. Adjusted\* Odds Ratios for Reporting Active\*\* Urgency or UI Symptoms at the 12-Month Follow-Up Survey Among Males and Females Who Reported Active Urgency or UI Symptoms at Baseline, GLOBE Study, 2008

Variable	Category	Males				Females			
		Urgency (n = 947)		Urinary incontinence (n = 472)		Urgency (n = 1,194)		Urinary incontinence (n = 999)	
		Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
Active baseline urgency		1.35	1.24–1.48			1.36	1.24–1.48		
Active baseline incontinence				1.51	1.25–1.83			1.51	1.31–1.74
Age	40–49	1.00	—	1.00	—	1.00	—	1.00	—
	50–59	1.41	0.84–2.36	1.01	0.48–2.14	1.65	1.05–2.59	1.20	0.77–1.88
	60–69	1.06	0.63–1.77	0.92	0.43–1.95	2.38	1.37–4.12	2.00	1.13–3.53
	70+	1.73	1.03–2.91	1.65	0.79–3.43	1.64	0.98–2.75	1.34	0.81–2.22
Marital status	Married	1.00	—	1.00	—	1.00	—	1.00	—
	Never married	0.89	0.42–1.92	0.85	0.32–2.24	0.75	0.33–1.69	1.27	0.56–2.89
	Divorced/sep	1.80	0.93–3.49	2.09	0.87–5.00	0.95	0.55–1.64	0.56	0.89–2.74
	Widowed	1.78	0.78–4.11	1.96	0.78–4.91	0.96	0.58–1.59	1.23	0.73–2.08
Education	<HS Diploma	1.00	—	1.00	—	1.00	—	1.00	—
	HS Diploma/GED	0.77	0.39–1.49	0.70	0.31–1.59	0.66	0.33–1.30	0.64	0.33–1.26
	Some college	0.47	0.24–0.94	0.51	0.22–1.18	0.62	0.30–1.29	0.67	0.33–1.38
	College grad+	0.56	0.28–1.13	0.85	0.35–2.10	0.41	0.20–0.85	0.43	0.21–0.90
Body mass index	<25	1.00	—	1.00	—	1.00	—	1.00	—
	25–29.99	0.93	0.58–1.48	2.34	1.26–4.33	1.29	0.84–1.99	1.35	0.89–2.04
	30+	1.21	0.74–1.99	2.30	1.21–4.36	0.97	0.64–1.47	1.93	1.27–2.93
UTI in past 4 weeks	No (ref)	1.00	—	1.00	—	1.00	—	1.00	—
	Yes	0.83	0.32–2.13	0.48	0.18–1.31	1.00	0.48–2.10	1.18	0.48–2.89
Duration since onset of symptoms	Missing	1.00	—	1.00	—	1.00	—	1.00	—
	< 6 months	4.03	2.36–6.88	10.0	2.81–35.6	3.07	1.85–5.10	4.05	1.63–10.06
	6–12 months	5.25	2.94–9.38	16.7	4.73–59.1	3.02	1.71–5.32	8.07	3.22–20.24
	1–2 years	5.43	3.14–9.39	21.1	6.30–70.7	2.99	1.79–4.98	8.30	3.47–19.85
	3–5 years	4.03	2.41–6.72	19.79	5.89–66.5	4.72	2.54–8.79	9.69	4.00–23.49
	>5 years	4.36	2.35–8.09	17.6	5.08–60.8	3.47	1.85–6.54	10.93	4.42–27.02
Parity						1.00	—	1.00	—
	1					1.06	0.51–2.21	2.58	1.24–4.95
	2					0.67	0.37–1.23	1.76	0.97–3.20
	3+					0.89	0.49–1.63	2.50	1.37–4.55

\*Odds ratios adjusted for age, marital status, education, BMI, UTI in past 4 weeks, duration of symptoms, parity (females only).

\*\*Active urgency = urgency symptoms score ≥3. Active incontinence = incontinence symptom score ≥2.

In logistic regression analysis of those with no active urgency at baseline (i.e., urgency score <3) (Table V), the adjusted odds of having urgency symptoms at 12 months were associated with older age (males only), marriage (females only), higher BMI, and parity (i.e., one birth vs. none). Among those with no UI symptoms at baseline (i.e., UI score <2), the odds of having UI symptoms at 12 months were associated with older age (males only), never being married (females only), no high school diploma (statistically significant among females and a similar non-significant trend among males), and BMI (females only). While the odds ratios for active UI at 12 months were elevated among females with one or more births, none were statistically significant.

DISCUSSION

The findings from this study indicate that intra- and inter-individual expression of bladder control symptoms is highly variable in the general population. A majority of individuals who appear to have urgency or UI symptoms at one point in time report that the symptoms occur less than once a week. This finding and the strong associations of change in symptom status with duration of time with symptoms have implications for inclusion criteria in treatment trials and possibly for the types of treatments that may appeal to those with bladder control symptoms.

Among those with active symptoms at baseline, our data indicate that UI episodes occur once a week or less for a majority of UI cases and for almost 40% of those with urgency. In contrast, 15–26% of urgency and UI cases reported symptoms occurring from a few times a week to every day. This distribution of episode frequency represents a single 4-week snapshot. Those with active symptoms at baseline do not fully represent all potential active cases when longitudinal data are considered. Among individuals with no urgency symptoms at baseline, 22% had urgency symptoms at 12 months. Among individuals with no UI symptoms at baseline, 13% had UI symptoms 12 months later. However, both of the latter subgroups with active symptoms at follow-up had mean urgency (4.31, SD 1.79) and UI scores (2.59, SD 0.97), that were substantially lower than their counterparts who had persistent symptoms at baseline and follow-up (urgency 6.36, SD 2.75; UI 3.48, SD 1.44). This pattern was expected given the variability in symptoms over time. That is, a significant proportion of those with bladder control symptoms will transition in and out of periods with active symptoms.

The longitudinal data indicate that change from active to inactive symptoms (i.e., urgency score <3, UI score <2) is common; only 7% of-the-population report UI symptoms every day at baseline and at follow-up. The frequency with which bladder control symptoms occurs in the general population parallels what has been observed for a variety of

TABLE V. Adjusted\* Odds Ratios for Reporting Active\*\* Urgency/UI Symptoms at the 12-Month Follow-Up Survey Among Males and Females Who Reported No Urgency/UI Symptoms at Baseline, GLOBE Study, 2008

Variable	Category	Males				Females			
		Urgency (n = 1,123)		Urinary incontinence (n = 1,593)		Urgency (n = 1,390)		Urinary incontinence (n = 1,558)	
		Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
Age	40–49	1.00	—	1.00	—	1.00	—	1.00	—
	50–59	2.01	1.16–3.49	1.27	0.74–2.17	0.85	0.60–1.22	1.10	0.74–1.61
	60–69	2.33	1.34–4.06	1.26	0.72–2.19	0.89	0.60–1.32	0.87	0.56–1.35
	70+	3.84	2.24–6.57	2.03	1.20–3.43	0.70	0.46–1.06	1.10	0.71–1.73
Marital status	Married	1.00	—	1.00	—	1.00	—	1.00	—
	Never married	1.24	0.65–2.34	0.86	0.40–1.84	2.25	1.15–4.38	2.28	1.15–4.51
	Divorced/sep	0.52	0.26–1.01	0.68	0.40–1.15	2.17	1.46–3.21	0.78	0.48–1.29
	Widowed	0.85	0.43–1.70	0.85	0.49–1.47	1.05	0.69–1.60	1.03	0.67–1.57
Education	<HS Diploma	1.00	—	1.00	—	1.00	—	1.00	—
	HS Diploma/GED	1.39	0.82–2.36	0.68	0.40–1.15	1.12	0.67–1.88	0.57	0.35–0.93
	Some college	1.08	0.61–1.99	0.85	0.49–1.47	0.99	0.67–1.73	0.55	0.32–0.95
	College grad+	0.68	0.37–1.23	0.58	0.33–1.04	0.77	0.44–1.37	0.67	0.39–1.15
Body mass index	<25	1.00	—	1.00	—	1.00	—	1.00	—
	25–29.99	1.09	0.74–1.62	0.92	0.61–1.39	1.62	1.17–2.23	1.19	0.84–1.67
	30+	1.66	1.09–2.54	1.10	0.71–1.72	1.97	1.42–2.74	1.51	1.07–2.14
UTI in past 4 weeks	No (ref)	1.00	—	1.00	—	1.00	—	1.00	—
	Yes	0.81	0.43–1.70	2.40	0.76–7.54	0.30	0.07–1.32	1.73	0.84–3.58
Parity						1.00	—	1.00	—
	1					2.18	1.30–3.64	1.74	0.67–3.11
	2					0.99	0.61–1.62	1.51	0.88–2.58
	3+					1.55	0.95–2.51	1.58	0.92–2.70

\*Odds ratios adjusted for age, marital status, education, BMI, UTI in past 4 weeks, parity (females only).

\*\*Active urgency = urgency symptoms score  $\geq 3$ . Active incontinence = incontinence symptom score  $\geq 2$ .

common chronic episodic conditions (e.g., headache, asthma, GERD).<sup>11–14</sup> For these other conditions, a relatively small proportion of active cases have symptoms that occur every other day or every day. For example, 85% of the general population reports headaches in the previous year; only 4% report persistent headache frequency (i.e., 15+ days per month) lasting 6 months or more.<sup>21</sup> Even among those with persistent headache, most transition to a less frequent symptom state.<sup>16</sup>

The parallels with other symptomatic conditions strongly suggests that bladder control is largely a chronic episodic condition, where transitions between episodes of more and less frequent and severe symptom states, including the complete absence of symptoms, are commonplace. This pattern has been reported in previous longitudinal studies of bladder control symptoms.<sup>18,22,23</sup> For example, Moller et al.<sup>22</sup> reported that more than half of women age 40–60 reporting that UI symptoms occurred daily at baseline reported less frequent UI episodes at 12 months.

Preventive treatments are prescribed for those who have other chronic episodic conditions (e.g., migraine, asthma) when the frequency of episodes is high, whereas acute rescue treatments are prescribed for those with either low- or high-frequency episodes. Most urgency and UI cases in the general population experience infrequent symptoms that come and go. This may explain why most patients who are prescribed an anti-muscarinic do not take it long term.<sup>24–26</sup> It may be sensible to consider treatment models where both acute rescue medications and preventive medications are used alone or in combination depending on the individual's current symptom status.

In general, our data indicate that urgency episodes are less frequent in males than in females. Moreover, males had urgency symptoms, on average, for a significantly shorter

period of time than did females. Within duration categories, the mean urgency score was consistently higher for females than for males. The shorter duration of time with symptoms may indicate that males have a later age of onset, as previously suggested,<sup>10</sup> and possibly a higher remission rate than females as previously reported by Herzog et al.<sup>18</sup> The fact that males are less likely to express symptoms at follow-up is consistent with a higher remission rate. Continued follow-up of the current cohort should reveal whether remission rates are higher for males than for females.

Duration of time with bladder control problems was a strong predictor of symptom frequency and variability in symptom expression over time. Our data indicate that those who report urgency and UI for 1 year or more have considerably higher mean symptom scores and are more likely to have active symptoms at follow-up. Because transient non-pathophysiologic occurrence of urgency symptoms may be relatively common in the general population, validity of case criteria for urgency may improve by requiring that individuals report having symptoms for 6–12 months or more.

Individuals who reported urgency symptoms but who were missing duration data comprise a substantial proportion of all individuals who reported urgency symptoms. The mean urgency score for this subgroup was lower than that of all other duration subgroups and this subgroup was less likely to report having symptoms at 12-month follow-up. Moreover, individuals with elevated urgency scores who were missing urgency duration responses were younger, more likely to be male, and have a lower BMI than those who reported duration of time with symptoms. Similarly, individuals who did not report a duration value for urine loss symptoms were more likely to be male and have a lower BMI. However, the latter group was older than responders and were less educated than individuals with urine loss duration responses. In general, this

pattern suggests that those who did not report duration of time with symptoms had a lower risk profile for bladder control problems. The duration question was worded such that individuals had to recognize they had urgency, otherwise the question was skipped. Continued follow-up of this subgroup will help to determine whether these respondents largely comprised true urgency cases who are more likely to have transient remission or whether the urgency symptoms in this subgroup are more like those in the general population who do not have urgency. A considerably smaller proportion of those with UI did not self-recognize their condition. This may be explained by the more overt nature of urine loss compared to urgency.

The variability in symptom expression observed in our longitudinal study may explain, in part, the large placebo effect observed in randomized clinical trials (RCT) for UI. RCT placebo response to treatment of UI range from 32% to 64% have been attributed to patient behavior (e.g., awareness of voiding behavior, risk factors), selection criteria, the trial design, and the duration of observation.<sup>27</sup> Our data suggest that for any given 4-week period, a substantial percentage of UI cases will not express symptoms or will experience a reduction in symptom frequency or severity. Placebo responses may be reduced by identifying predictors of persistent symptoms. For example, UI cases with new onset are likely to have highly variable symptom frequency over time. In contrast, a longer duration of time with UI predicts more persistent UI symptoms. Alternative strategies may also need to be considered to reduce the placebo effect, including longer observation periods and treatment protocols that are recursive, where stopping and starting a treatment during the course of a trial is linked to symptom status.

The participation rate of 44% in our study is a potential limitation. In particular, selective participation of those with bladder control symptoms at the time of the survey or more persistent symptoms could result in an overestimate of symptom prevalence at cross-section. However, our primary focus in this study is on temporal variability in symptom expression, not prevalence of symptoms at a given point in time. As such, selective participation is largely a concern if those with more persistent symptoms were more likely to participate. This type of selection would mean that we have underestimated variability in symptoms (i.e., as those with greater variability in symptoms would be under-represented) in the general population, a notion that places even greater emphasis on the need to consider episodic treatment and on management of placebo responses in clinical trials.

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