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Modifiers of response to treatment with fesoterodine for urgency-predominant urinary incontinence in a randomized controlled trial

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Abstract

Objective—To identify clinical and demographic characteristics that moderate response to treatment with fesoterodine among women diagnosed with urgency-predominant urinary incontinence (UUI).

Methods—A multicenter, double-blinded, 12-week randomized controlled trial of pharmacologic therapy for urgency-predominant urinary incontinence in community-dwelling women diagnosed by the 3-item Incontinence Questionnaire (3IQ) was previously performed. Participants (N = 645) were randomized to fesoterodine therapy (4–8 mg daily; N=322) or placebo (N=323). Urinary incontinence was assessed by 3-day voiding diaries. In this secondary analysis, a “responder” was defined as 50% reduction in overall incontinence episode frequency compared to baseline.

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Clinical and demographic characteristics that may moderate treatment response were assessed by testing for interaction between characteristics and intervention in logit models of responders, adjusting for clinical site.

Results—Participants were mean (SD) 56 (± 14) years old, 68% were white race, and had 3.9 (± 3.0) urgency incontinence episodes per day. There were no baseline differences in demographic, clinical or incontinence characteristics between treatment and placebo groups or between responders and non-responders. There was an increase in the proportion of responders to fesoterodine with increasing age ($p=0.04$) and parity (0.04), and among married women ($p=0.03$), but no effect modification was observed by race/ethnicity, body mass index, education, employment status, alcohol or tobacco use.

Conclusions—In ambulatory women with UUI, older age, being married, and higher parity significantly moderated and potentiated the effects of pharmacologic therapy on incontinence frequency. This study identifies certain populations who may have increased responsiveness to treatment with antimuscarinic therapy and may be used to inform and guide future therapy.

Keywords

Urgency urinary incontinence; fesoterodine; predictors of treatment response

INTRODUCTION

Urinary incontinence is common among women in the United States with an overall prevalence of 10–15%¹ and as high as 77% in some populations such as elderly patients or those with cognitive dysfunction². While urinary incontinence is not generally associated with an increased mortality,³ it can have significant adverse impact on quality of life, sexual function, medical morbidity and caregiver burden. A simple 3-item self-administered questionnaire, the 3 Incontinence Questionnaire, (3IQ) has been demonstrated to be an effective measure to both identify women with urgency-predominant urinary incontinence (UUI) and to facilitate initiation of pharmacologic treatment without further clinical evaluation.⁴ This study showed that among ambulatory women with UUI diagnosed with the 3IQ, there was a significant reduction in urinary incontinence episodes at 12 weeks with pharmacological treatment compared to a placebo control group, without an increase in adverse events.⁴

There is a lack of knowledge about the use of antimuscarinics in the general population. Many clinical trials have demonstrated the efficacy of antimuscarinic medications to treat UUI, yet there are limited data on effectiveness in different patient populations. Clinical trials for pharmacological therapy typically include subgroup analyses stratified by age and gender, but generally do not provide comprehensive information about the effect of additional demographic and clinical characteristics. While studies of the general population may provide information with better clinical applicability, the heterogeneity of the sample makes analysis difficult. We therefore felt that a secondary analysis of a clinical trial with specific including and exclusion criteria would provide valuable information.

The goal of this study was to identify clinical and demographic characteristics that moderate pharmacologic treatment response among women diagnosed with UUI identified by the 3IQ. This may facilitate predicting good and/or poor response to streamlined pharmacological therapy initiation with the 3IQ and help to inform to patients' expectation of treatment. The investigation involves a secondary analysis of a previously published study.⁴

MATERIAL AND METHODS

Participants

A multicenter, double-blinded, 12-week randomized trial of pharmacological therapy and placebo control for urgency-predominant incontinence in women diagnosed by the simple 3IQ was previously performed.⁴ Participants were community-dwelling, ambulatory women at least 18 years old recruited at 13 clinical sites in the United States. Complete study methods and results were previously published.⁴ In brief, the study population included women with urgency or mixed urgency predominant urinary incontinence with at least three episodes of urgency urinary incontinence on a 3-day bladder diary. Women were excluded if they self-reported complex medical histories that would require a specialist evaluation for incontinence before initiating pharmacological therapy. Participants were assigned randomly to fesoterodine 4-8mg daily or identical-appearing placebo. All participants were asked to not initiate other pharmacologic incontinence treatments and pelvic floor or bladder physical therapy for the 12-week trial period. According to previously established protocols for participant-directed dosing, participants were started initially on fesoterodine 4 mg and offered the option of increasing their dose to fesoterodine 8 mg at 2, 4, and 8 weeks with maximum of 8 or minimum of 4 mg daily.

Measures

At the initial visit, participants completed the 3IQ and questionnaires on demographic characteristics (e.g., age, race or ethnicity, education), habits (e.g., smoking, alcohol consumption), medication use, and reproductive (e.g., parity, menopause status), medical (e.g., diabetes, hypertension, stroke, chronic liver disease), surgical (e.g., previous hysterectomy) and incontinence (e.g., age of onset of incontinence, and duration (in years) of incontinence) histories. Physical examination included body mass index measurement, a thorough pelvic exam, basic neurologic examination, and cough stress test and measurement of post void residual volume and urine analysis were performed⁴. At baseline and 12 weeks, women also completed a validated 3-day voiding diary including number of voids, incontinence episode by type (urgency, mixed, other), and sensation of urgency (rated as none, mild, moderate, or severe). Participants completed the Patient Perception of Bladder Condition (PPBC), a validated single-item global measure of patients' subjective impression of their current urinary problems.⁵ Participants also completed the Overactive Bladder Questionnaire (OAB-q), a 33-item, condition-specific measure designed to assess the impact of OAB symptoms⁶

Statistical Analysis

Baseline characteristics of participants in each treatment group and of responders and non-responders were compared using chi-square or kruskal-wallis tests. Baseline urinary

incontinence episodes were compared using analysis of variance (ANOVA) models. At 12 weeks, a therapeutic responder was defined by 50% reduction in incontinence-episode frequency (all types) from baseline, a clinically meaningful threshold for incontinence improvement.^{7, 8} Conversely, a non-responder was defined by less than 50% reduction in incontinence-episode frequency from baseline. Moderation by clinical and demographic characteristic was assessed by testing interaction terms between each clinical characteristic and intervention in logit models of responders adjusted for clinical site. A P value <0.05 was considered significant. Analyses were performed in SAS 9.4 (SAS Institute, Cary, NC).

RESULTS

A total of 645 participants were randomly assigned to fesoterodine therapy (N=322) or placebo (N=323). Follow-up at 12 weeks was similar between groups (fesoterodine N=271, 82% and control N=278, 86%). At baseline among the 549 participants with 12-week follow-up data, mean (SD) age was 56 ($\pm$ 14) years, 66% were white race, and women reported 3.9 ($\pm$ 3.0) urgency incontinence episodes per day (Table 1). Baseline characteristics did not differ significantly between the two treatment groups, nor did they differ between responders and non-responders (data not shown). There were also no differences in baseline incontinence episode frequency between responders and non-responders when stratified by age, BMI, race/ethnicity, education, relationship status, employment, alcohol use, smoking status, menopausal status, gravidity or parity (data not shown).

Response to pharmacological treatment at 12-weeks was moderated by several clinical and demographic characteristics including age, marital status, education, parity and incontinence type (Table 2). There was an increase in the proportion of responders to fesoterodine with increasing age ($p=0.04$). The treatment effect was non-significant below age 45 years, but increasingly stronger with age above 45 years. Among participants aged 18–28 years treated with fesoterodine, 48% were therapeutic responders compared to 76% of women aged 75 years. An inverse trend was seen among women in the placebo group, with more younger women responding to placebo treatment (60%) than older women (31%). Similarly, an increase in responders to fesoterodine among participants who were married or living as married (74%) compared to single women (68%; $p=0.03$), and an inverse relationship in the placebo arm, with response rate among married women lower than for single women (44% vs. 57%, respectively, $p=0.03$) was noted. Education had a complex relationship with treatment response but did demonstrate significant effect modification ($p=0.03$). Increasing parity was associated with higher responder rate ($p=0.04$). Finally, urgency urinary incontinence type modified treatment response, with 74% of women with pure UUI achieving therapeutic response compared to 68% with urgency-predominant mixed urinary incontinence ($p=0.04$). We observed no modification of treatment response by race/ethnicity, BMI, employment status, alcohol or tobacco use, or menopausal status.

DISCUSSION

In this secondary analysis of a previously published randomized, controlled trial of pharmacological therapy for UUI, age, marital status and parity were all significant modifiers that potentiate the effects of treatment with fesoterodine. To our knowledge this is

the first analysis of data from randomized trial that provides data allowing a comprehensive evaluation of clinical and demographic predictors of treatment response to pharmacologic treatment of UUI.

Prior pharmacokinetic studies of antimuscarinic drugs for UUI have demonstrated that increasing age is often associated with more frequent and significant side effects including dry mouth, blurry vision, sedation and confusion.⁹ Phase 2 and phase 3 placebo-controlled efficacy and safety studies of fesoterodine showed the incidence of treatment-associated adverse events, including dry mouth, constipation, dyspepsia, increase in residual urine, dizziness (at 8 mg only) and urinary tract infection, was higher in women 75 years of age and older compared to younger women.^{10–13} The active metabolite of fesoterodine, 5-hydroxymethyl tolterodine, is known to undergo extensive metabolism and clearance by the liver. In elderly patients, many drugs demonstrate an exaggerated response secondary to decreased drug metabolism and clearance.¹⁴ Perhaps this pharmacokinetic difference among older participants explains the observed effect modification in this study.

There are conflicting data on the change in pharmacologic efficacy with increased age. Phase 2 and phase 3 placebo-controlled efficacy and safety studies of fesoterodine showed no overall differences in efficacy between participants younger compared to older than 65 years of age. However, in a post hoc analysis of data from a fixed-dose trial of fesoterodine stratified by age, fesoterodine 4 and 8 mg improved symptoms significantly more than placebo in participants younger than 65 years and in a group aged 65–74 years; only fesoterodine 8mg was effective in participants aged 75 years and older.¹³ There has been one randomized controlled trial of a drug from the same class that looked specifically at the geriatric population observing that overall efficacy in an older population was greater than efficacy noted in prior studies of the general population.¹⁵

There are limited data reporting on other demographic characteristics and response to treatment by antimuscarinic medications. In phase 1 placebo-controlled trials there was no difference in the pharmacokinetics of fesoterodine between different racial groups suggesting similar levels of efficacy. Studies of other antimuscarinic agents including solifenacin^{16, 17} and tolterodine tartrate,¹⁸ however, concluded that the number of subjects of different races studied in phase 1 trials was not adequate to make any conclusions on the effect of race on the pharmacokinetics of these antimuscarinic drugs. Prior efficacy studies of fesoterodine have not commented specifically on differences in efficacy between racial groups and the studies likely have limited power due to sample size.

Increased parity was also associated with greater likelihood of treatment response, which may suggest that there is some physiologic change brought on by pregnancy/delivery that affects the efficacy of therapy. Perhaps the pathophysiologic mechanism of UUI is different among parous women compared to nulliparous women. We are unclear why there was a difference in treatment response based on marital status and marital status has not been studied in similar drug trials. It is possible that marital status was a marker for other unmeasured socioeconomic (or other) characteristics that modified treatment response, or this may be a spurious finding.

While age and marital status were associated with increased efficacy in the treatment group, we noted an inverse relationship in the placebo group with age and marital status associated with decreased response. Studies of drugs in other fields of medicine including depression¹⁹ epilepsy²⁰ and migraines²¹ have noted significantly increased placebo response among younger respondents and have suggested that the response to placebo may be dependent on the age of patients. Effect modification by the type of incontinence is logical since fesoterodine is a drug that specifically treats UUI. A higher percentage of women with pure urgency incontinence compared to mixed urgency incontinence achieved a therapeutic treatment response.

In addition to understanding the relationship between demographic characteristics and treatment efficacy, it is also important to understand which patients may be at risk for treatment failure. Data from this study suggest that younger patients and nulliparous patients may benefit from evaluation by a specialist given the lower frequency of therapeutic responders. Clinical and demographic characteristics associated with pharmacological treatment failure may help predict which patients warrant more thorough evaluation and streamline diagnostic testing and treatment choice.

The major strengths of this study include that the data was collected from a multi-center, randomized, placebo-controlled trial with comprehensive evaluation of demographic and clinical characteristics. However, we acknowledge several limitations. This study involves a secondary analysis which the primary study was not powered to assess which may explain the lack of associations with several demographic strengths. This study looked specifically at urgency-predominant urinary incontinence and excluded patients with stress only or stress-predominant mixed incontinence or those with urinary urgency in the absence of incontinence. This study also excluded participants with major comorbidities that might warrant further evaluation by a specialist prior to initiation of pharmacologic therapy. Therefore, our population may not be entirely generalizable. Finally, this study involved the use of one antimuscarinic drug and there are several similar drugs that work through similar mechanism of action. It would be reasonable to assume that the effect modification would be similar for drugs in the same general class, but further studies are clearly needed before making definitive statements.

In conclusion, this study provides evidence to identify certain subpopulations that may be more responsive to treatment with antimuscarinic therapy, in particular women who are older, parous, married or report urgency only incontinence. By identifying demographic characteristics associated with a better clinical response, primary care providers can better select those patients that may benefit from initial treatment.

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REFERENCES

1. Lawrence JM, Lukacz ES, Nager CW, Hsu J-WY, Luber KM. Prevalence and co-occurrence of pelvic floor disorders in community-dwelling women. *Obstet Gynecol.* 2008; 111:678–685. [PubMed: 18310371]
2. Offermans MPW, Du Moulin MFMT, Hamers JPH, Dassen T, Halfens RJG. Prevalence of urinary incontinence and associated risk factors in nursing home residents: a systematic review. *Neurourol Urodyn.* 2009; 28:288–294. [PubMed: 19191259]
3. Herzog AR, Diokno AC, Brown MB, Fultz NH, Goldstein NE. Urinary incontinence as a risk factor for mortality. *J Am Geriatr Soc.* 1994; 42(3):264–268. <http://www.ncbi.nlm.nih.gov/pubmed/8120310>. [PubMed: 8120310]
4. Huang AJ, Hess R, Arya LA, et al. Pharmacologic treatment for urgency-predominant urinary incontinence in women diagnosed using a simplified algorithm: A randomized trial. *Am J Obstet Gynecol.* 2012; 206
5. Coyne KS, Matza LS, Kopp Z, Abrams P. The validation of the patient perception of bladder condition (PPBC): a single-item global measure for patients with overactive bladder. *Eur Urol.* 2006; 49(6):1079–1086. [PubMed: 16460875]
6. Coyne K, Revicki D, Hunt T, et al. Psychometric validation of an overactive bladder symptom and health-related quality of life questionnaire: the OAB-q. *Qual Life Res.* 2002; 11(6):563–574. <http://www.ncbi.nlm.nih.gov/pubmed/12206577>. [PubMed: 12206577]
7. Yalcin I, Peng G, Viktrup L, Bump RC. Reductions in stress urinary incontinence episodes: What is clinically important for Women? *Neurourol Urodyn.* 2009 n/a-n/a.
8. Campbell JD, Gries KS, Watanabe JH, Ravelo A, Dmochowski RR, Sullivan SD. Treatment success for overactive bladder with urinary urge incontinence refractory to oral antimuscarinics: a review of published evidence. *BMC Urol.* 2009; 9:18. [PubMed: 19930578]
9. No Title.
10. Yamaguchi O, Nishizawa O, Takeda M, et al. Efficacy, Safety and Tolerability of Fesoterodine in Asian Patients with Overactive Bladder. *Low Urin Tract Symptoms.* 2011; 3(1):43–50. [PubMed: 26676351]
11. Chapple C, Van Kerrebroeck P, Tubaro A, et al. Clinical efficacy, safety, and tolerability of once-daily fesoterodine in subjects with overactive bladder. *Eur Urol.* 2007; 52(4):1204–1212. [PubMed: 17651893]
12. Nitti VW, Dmochowski R, Sand PK, et al. Efficacy, safety and tolerability of fesoterodine for overactive bladder syndrome. *J Urol.* 2007; 178(6):2488–2494. [PubMed: 17937959]
13. Kraus SR, Ruiz-Cerdá JL, Martire D, Wang JT, Wagg AS. Efficacy and tolerability of fesoterodine in older and younger subjects with overactive bladder. *Urology.* 2010; 76(6):1350–1357. [PubMed: 20974482]
14. Delafuente JC. Pharmacokinetic and pharmacodynamic alterations in the geriatric patient. *Consult Pharm.* 2008; 23(4):324–334. <http://www.ncbi.nlm.nih.gov/pubmed/18454589>. [PubMed: 18454589]
15. Chapple C, DuBeau C, Ebinger U, Rekedal L, Viegas A. Darifenacin treatment of patients ≥ 65 years with overactive bladder: results of a randomized, controlled, 12-week trial. *Curr Med Res Opin.* 2007; 23(10):2347–2358. [PubMed: 17706004]
16. Smulders RA, Krauwinkel WJ, Swart PJ, Huang M. Pharmacokinetics and safety of solifenacin succinate in healthy young men. *J Clin Pharmacol.* 2004; 44(9):1023–1033. [PubMed: 15317830]
17. Chapple CR, Rechberger T, Al-Shukri S, et al. Randomized, double-blind placebo- and tolterodine-controlled trial of the once-daily antimuscarinic agent solifenacin in patients with symptomatic overactive bladder. *BJU Int.* 2004; 93(3):303–310. <http://www.ncbi.nlm.nih.gov/pubmed/14764127>. [PubMed: 14764127]

18. Brynne N, Stahl MM, Hallén B, et al. Pharmacokinetics and pharmacodynamics of tolterodine in man: a new drug for the treatment of urinary bladder overactivity. *Int J Clin Pharmacol Ther*. 1997; 35(7):287–295. <http://www.ncbi.nlm.nih.gov/pubmed/9247842>. [PubMed: 9247842]
19. Rutherford BR, Roose SP. A model of placebo response in antidepressant clinical trials. *Am J Psychiatry*. 2013; 170(7):723–733. [PubMed: 23318413]
20. Rheims S, Cucherat M, Arzimanoglou A, Ryvlin P. Greater response to placebo in children than in adults: a systematic review and meta-analysis in drug-resistant partial epilepsy. *PLoS Med*. 2008; 5(8):e166. [PubMed: 18700812]
21. Rothner AD, Wasiewski W, Winner P, Lewis D, Stankowski J. Zolmitriptan oral tablet in migraine treatment: high placebo responses in adolescents. *Headache*. 2006; 46(1):101–109. [PubMed: 16412157]

Table 1

Clinical and demographic characteristics of participants

Characteristic	All N=549	Placebo N=278	Fesoterodine N=271	P-Value
Age (years) - no. (%)				
18–29	36 (6.6)	15 (5.5)	21 (7.6)	0.10
30–44	62 (11.3)	28 (10.3)	34 (12.2)	
45–59	211 (38.4)	119 (43.9)	92 (33.1)	
60–74	189 (34.4)	83 (30.6)	106 (38.1)	
≥75	51 (9.3)	26 (9.6)	25 (9.0)	
Race/Ethnicity - no. (%)				
Asian	14 (2.6)	6 (2.2)	8 (2.9)	0.70
Black/African American	117 (21.3)	57 (21.0)	60 (21.6)	
Native American/American Indian	1 (0.2)		1 (0.4)	
Latina/Hispanic	35 (6.4)	20 (7.4)	15 (5.4)	
White/Caucasian	373 (67.9)	185 (68.3)	188 (67.6)	
Multiethnic or Mixed Race	9 (1.6)	3 (1.1)	6 (2.2)	
Married or living as married - no. (%)	247 (45.0)	118 (43.5)	129 (46.4)	0.50
Education - no. (%)				
6th to 11th grade	18 (3.3)	12 (4.4)	6 (2.2)	0.04
High School Graduate	69 (12.6)	30 (11.1)	39 (14.0)	
Some College	206 (37.5)	113 (41.7)	93 (33.5)	
College Degree (4 year)	151 (27.5)	75 (27.7)	76 (27.3)	
Graduate or Professional Degree	105 (19.1)	41 (15.1)	64 (23.0)	
Employment status - no. (%)				
Employed in a job or business	243 (44.3)	124 (45.8)	119 (42.8)	0.70
Engaged (housework)	72 (13.1)	33 (12.2)	39 (14.0)	
Self-employed	45 (8.2)	24 (8.9)	21 (7.6)	
Volunteer Work	23 (4.2)	14 (5.2)	9 (3.2)	
Unemployed	60 (10.9)	27 (10.0)	33 (11.9)	
Retired	106 (19.3)	49 (18.1)	57 (20.5)	
Total household income - no. (%)				
< \$20k	116 (22.3)	56 (22.2)	60 (22.4)	0.66
\$20–<\$40k	117 (22.5)	62 (24.6)	55 (20.5)	
\$40–<\$60k	89 (17.1)	38 (15.1)	51 (19.0)	
\$60–<\$80k	74 (14.2)	38 (15.1)	36 (13.4)	
\$80–<\$100k	34 (6.5)	15 (6.0)	19 (7.1)	
\$100–<\$120k	28 (5.4)	16 (6.3)	12 (4.5)	
≥\$120k	62 (11.9)	27 (10.7)	35 (13.1)	
Current weekly alcohol consumption - no. (%)	174 (31.7)	86 (31.7)	88 (31.7)	0.98
Current cigarette smoking - no. (%)	76 (13.9)	37 (13.7)	39 (14.0)	0.91
Number of births (parity) - no. (%)				
0	113 (20.6)	56 (20.7)	57 (20.5)	0.67

Characteristic	All N=549	Placebo N=278	Fesoterodine N=271	P-Value
1	99 (18.0)	53 (19.6)	46 (16.5)	
2	165 (30.1)	83 (30.6)	82 (29.5)	
3+	172 (31.3)	79 (29.2)	93 (33.5)	
Not currently menstruating - no. (%)	397 (72.6)	199 (73.7)	198 (71.5)	0.56
Incontinent Episodes per day				
Total - mean (SD)	4.61 (3.3)	4.73 (3.2)	4.49 (3.4)	
Median (range)	3.7 (1.0–25.3)	4.0 (1.0–25.3)	3.3 (1.0–21.0)	0.07
Urgency - mean (SD)	3.89 (2.9)	3.96 (2.9)	3.81 (2.9)	
Median (range)	3.0 (1.0–25.3)	3.0 (1.0–25.3)	3.0 (1.0–18.7)	0.24
Type of incontinence - no. (%)				
Urgency Only	272 (49.5)	132 (48.7)	140 (50.4)	0.70
Mixed	277 (50.5)	139 (51.3)	138 (49.6)	

Table 2

Association of response to pharmacologic treatment and clinical and demographic characteristics

Demographic characteristics (moderators)	% Responders (50% reduction)		Logistic Model: Responder*	
	Placebo (n=271)	Fesoterodine (n=278)	Odds Ratio (95% CL) Fesoterodine vs Placebo	P-Value for Interaction of Moderator x Intervention
Age				
18–29	60%	48%	0.61 (0.16–2.32)	0.04
30–44	61%	65%	1.19 (0.42–3.34)	
45–59	54%	72%	2.18 (1.22–3.89)	
60–74	49%	75%	3.15 (1.70–5.84)	
≥75	31%	76%	7.12 (2.06–24.61)	
Race/Ethnicity				
Asian	33%	38%	1.20 (0.13–11.05)	0.42
Black/African American	51%	65%	1.79 (0.85–3.77)	
White/Caucasian/Native Am	51%	72%	2.50 (1.62–3.84)	
Latina/Hispanic	55%	93%	11.45 (1.25–104.60)	
Multiethnic/Mixed Race	67%	67%	1.00 (0.05–18.91)	
Relationship Status				
Not married	57%	68%	1.65 (1.03–2.64)	0.03
Married or living as married	44%	74%	3.55 (2.08–6.05)	
Education				
6th to 11th grade	50%	67%	2.00 (0.26–15.38)	0.02
High School Graduate	60%	56%	0.86 (0.33–2.27)	
Some College	48%	83%	5.26 (2.74–10.10)	
College Degree (4 year)	52%	67%	1.88 (0.97–3.64)	
Graduate or Professional Degree	54%	67%	1.77 (0.79–3.96)	
Employment				
Employed in a job or business	49%	67%	2.12 (1.26–3.56)	0.40
Engaged (housework)	55%	72%	2.12 (0.80–5.64)	
Self-employed	42%	86%	8.40 (1.94–36.43)	
Volunteer Work	36%	56%	2.25 (0.41–12.44)	
Unemployed	63%	67%	1.18 (0.41–3.41)	
Retired	57%	77%	2.54 (1.10–5.87)	
Total household income				
< \$20k	61%	72%	1.64 (0.75–3.56)	0.75
\$20–<\$40k	52%	67%	1.93 (0.91–4.09)	
\$40–<\$60k	42%	67%	2.75 (1.15–6.55)	
\$60–<\$80k	58%	78%	2.55 (0.92–7.03)	
\$80–<\$100k	33%	74%	5.60 (1.27–24.64)	
\$100–<\$120k	50%	83%	5.00 (0.82–30.46)	
≥\$120k	37%	63%	2.88 (1.02–8.13)	

Demographic characteristics (moderators)	% Responders (50% reduction)		Logistic Model: Responder*	
	Placebo (n=271)	Fesoterodine (n=278)	Odds Ratio (95% CL) Fesoterodine vs Placebo	P-Value for Interaction of Moderator x Intervention
Alcohol consumption				
No Alcohol	51%	73%	2.58 (1.68–3.97)	0.38
Weekly use of alcohol	51%	66%	1.85 (1.00–3.40)	
Smoker				
Non-smoker	50%	72%	2.54 (1.73–3.71)	0.16
Current smoker	62%	67%	1.22 (0.48–3.12)	
Number of births (parity)				
0	68%	72%	1.21 (0.54–2.72)	0.04
1	55%	65%	1.55 (0.69–3.50)	
2	46%	65%	2.16 (1.16–4.05)	
3+	43%	78%	4.83 (2.48–9.40)	
Menopause status				
Menstruating	59%	67%	1.41 (0.72–2.74)	0.09
Not currently menstruating	48%	72%	2.79 (1.84–4.23)	
Type of Incontinence				
Urge Only	45%	74%	3.34 (2.01–5.55)	0.05
Mixed	57%	68%	1.62 (0.99–2.65)	

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Adjusted for clinical site