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Associations of commonly-used medications with urinary incontinence in a community-based sample

Susan A. Hall¹, May Yang¹, Margaret A. Gates¹, William D. Steers, Sharon L. Tennstedt¹, and John B. McKinlay¹

¹New England Research Institutes, Nine Galen St., Watertown, MA 02472 USA

²Department of Urology, School of Medicine, University of Virginia, Charlottesville, VA 22908 USA

Abstract

Purpose—To examine the association between use of medications and prevalence of urinary incontinence (UI) in gender-specific analyses of a community-based, representative sample.

Materials and Methods—A population-based epidemiologic study was conducted among 5,503 men and women aged 30–79 residing in Boston, Massachusetts (baseline data collected 2002–2005). Urologic symptoms were ascertained in a two-hour, in-person interview. UI was defined as urine leakage occurring weekly or more often, considering the past year. Medications used in the past month were considered ‘current use’. Associations of 20+ medications and prevalent UI were examined using multivariable logistic regression (odds ratios [ORs] and 95% confidence intervals [CIs]) with adjustments for known UI risk factors.

Results—UI prevalence in the analysis sample was 9.0% in women and 4.6% in men. Among women, prevalence was highest among users of certain antihistamines (28.4%) and angiotensin II receptor blockers (ARBs) (22.9%). Among men, prevalence was highest among ARB (22.2%) and loop diuretic (19.1%) users. After final multivariable adjustment, there were significant positive associations for certain antihistamines, beta receptor agonists, ARBs, and estrogens with UI among women (all ORs >1.7), and a borderline-significant association for anticonvulsants (OR=1.75, 95% CI: 1.00, 3.07). Among men, only anticonvulsants (OR=2.50, 95% CI: 1.24, 5.03) were associated with UI after final adjustments, although ARBs showed an adjusted association of borderline significance (OR=2.21, 95% CI: 0.96, 5.10).

Conclusion—Although a cross-sectional analysis cannot determine causality, our analysis suggests certain medications should be further examined in longitudinal analyses of risk to determine their influence on urologic symptoms.

Keywords

medications; urinary incontinence; pharmacoepidemiology; epidemiology

Introduction

Recent evidence suggests that the already-substantial disease burden of urinary incontinence (UI) in the U.S. is increasing over time among both men and women.¹ The use of prescription medications is also increasing,² and is a commonly-accepted contributor to the population burden of UI as represented by the ‘DIAPPERS’ mnemonic (P for

¹Corresponding Author: Susan A. Hall, New England Research Institutes, 9 Galen St., Watertown, MA 02472 USA, Tel: 617-923-7747; fax 617-924-0968, shall@neriscience.com.

pharmaceuticals) for UI clinical investigation.³ Commonly-implicated medications include diuretics, antipsychotics, benzodiazepines, antidepressants, and hormone therapy in women.^{4, 5} However, despite the diversity of biologic mechanisms by which drugs may contribute to UI,^{4, 5} there are surprisingly few pharmacoepidemiologic investigations of the influence of medications on the prevalence or incidence of UI in light of new drug introductions in recent years as well as an increasing trend towards polypharmacy among older adults.² Our analytic goal was to examine the association of current use of commonly-used drugs and prevalent UI among men and women from a large community-based U.S. sample.

Materials and Methods

Study design and data collection

The Boston Area Community Health (BACH) Survey is an epidemiologic study conducted among 5,503 men and women aged 30-79 residing in Boston, Massachusetts; full study details are available.⁶ A multistage, stratified cluster sampling design was used to recruit approximately equal numbers from pre-specified age, race/ethnicity (black, Hispanic, white), and gender groups. This cross-sectional analysis used baseline data collected in 2002-2005 during a two-hour, in-person interview conducted by a trained, bilingual interviewer after acquisition of written informed consent. Interviews for 63.3% of eligible persons were completed, with a resulting study population of 2301 men and 3202 women (1767 black participants, 1877 Hispanic, 1859 white). All protocols and procedures were approved by the Institutional Review Board of New England Research Institutes.

Medications

Current medication use (within past four weeks) was collected by direct observation/recording of medication container labels and self-report with prompts for specific indications. Medication labels and/or responses were coded using the Slone Drug Dictionary, which classifies medications using a modification of the American Hospital Formulary Service Pharmacologic-Therapeutic Classification System.^{7, 8} Drug groups of interest were chosen *a priori* based on commonality of use⁹ or indication: antihypertensives (including diuretic subtypes), antilipemics, antidepressants, opiates/narcotics, benzodiazepines, COX-2 inhibitors, carboxyl-salicylate NSAIDS (e.g., aspirin), carboxyl-propionic NSAIDS (e.g., ibuprofen), estrogens, atypical antipsychotics, beta receptor agonists and synthetic corticosteroids. Exploratory analyses were conducted to identify additional drug groups with an unexpectedly high prevalence of use among persons with UI (medications identified in this step: sulfonylurea; non-benzodiazepine anticonvulsants including only carbamazepine, divalproex, gabapentin, levetiracetam, oxcarbazepine, primidone, tiagabine, and topiramate; histamine H2 antagonist and proton pump inhibitor anti-ulcer agents; and antihistamines including only cyproheptadine, desloratadine, fexofenadine, loratadine, and trimethobenzamide; hereinafter, 'antihistamines').

UI Definition

The presence or absence of UI was based on replies to: "Many people complain that they leak urine (wet themselves) or have accidents. In the last 12 months, have you leaked even a small amount of urine?" and "In the last 12 months, how often did you experience urinary leakage (wet yourself)?" Those reporting yes to the first question and a frequency of weekly or more often to the second question were considered to have UI; this identified cases with at least moderate severity on the validated Sandvik UI severity scale.¹⁰ Persons using medications for UI or benign prostatic hyperplasia (BPH) were included as UI cases if they were still reporting symptoms.

Covariates

Covariates were chosen based on prior documented associations with UI.¹¹ Women who reported having had a hysterectomy and/or bilateral oophorectomy were categorized as having surgical menopause. Depressive symptoms were considered present if at least five of eight symptoms on the abridged Center for Epidemiologic Studies Depression Scale were reported.¹² Other comorbidities were based on the question, “Have you ever been told by a health care provider that you have or had...?” Cardiac disease was a composite variable including coronary artery surgery, myocardial infarction, or angina. Body mass index was calculated from interviewer-measured weight and height and categorized as <30 kg/m² (non-obese) or 30+ kg/m² (obese). Socioeconomic status was constructed using standardized income and education variables for the Northeastern U.S. and reclassified into low, middle and high.¹³

Analytic sample and statistical analysis

Excepting models, all analyses were weighted for sampling design and conducted separately by gender using SAS v9.2 and SUDAAN v10.0.1. Weights were calculated for the sample obtained and account for non-response. The overall modeling goal was to evaluate associations between medication use and UI, adjusted for confounding variables. To avoid confounding by established urologic or neurologic conditions affecting bladder function, 482 subjects were removed from the analysis, leaving 5,021 persons (91.2% of the original sample). These 482 subjects gave 712 total reports of genitourinary cancers (129 reports), prolapsed bladder (90), bladder prostate surgery (231), UI surgery (83), a recommendation for catheter use (151), Parkinson’s disease (7) and multiple sclerosis (MS) (21). Missing data were replaced using 25 multiple imputations; <1% of data were missing for most variables. Medication variables were not imputed. Significant differences by UI status were tested using a chi-square test of association for categorical variables, or t-test for continuous variables. For each drug group, the prevalence of UI among users was estimated separately among men and women, and differences in prevalence among users and non-users tested using a chi-square test.

Finally, multivariable logistic regression modeling was used to estimate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for medication use (exposure) and prevalent UI (outcome). To reduce confounding, subpopulations of persons with antihypertensive indications (N=948 men, N=1199 women) and lipid-lowering drug indications (N=844 men, N=1188 women) were created for modeling analyses of these drug groups.¹⁴ Age- and race/ethnicity-adjusted models (‘minimally adjusted’ models) were first constructed separately by gender for each medication variable and UI. Additional covariates considered for parsimonious models were diabetes, cardiac disease, congestive heart failure, hypertension, high cholesterol, asthma, waist circumference and depression, plus arthritis, surgical menopause and 1+ vaginal delivery for women. To determine the structure of the final, parsimonious multivariable model, a model with all covariates was fit and variables backwards-selected, retaining only those covariates that induced a 12.5% change in the OR, or were significantly associated with the outcome (Wald F test $p < 0.10$). The influence of other medications was also considered in some multivariable models to evaluate the robustness of results.

Results

The overall prevalence of UI in the analysis sample (N=5,021) was 9.0% among women and 4.6% among men. Men and women with UI had significantly older mean age compared to those without (Table 1). Among women, there was a higher prevalence of diabetes, high cholesterol, hypertension, arthritis, asthma, obesity, and depressive symptoms among those

with UI compared to those without ($p < 0.05$). Women with UI were also more likely to have a higher mean waist circumference and to have given birth vaginally. Nearly half used 3 prescription medications compared to 28.1% of women without UI. Among men, there was a general pattern of higher comorbidities (especially diabetes, cardiac disease, and high cholesterol) among those with UI, but only having depressive symptoms was significantly different by UI status (28.9% with UI vs. 12.8% without, $p = 0.03$).

The prevalence of UI was examined within users of 25 medication groups, by gender (Table 2). Among women, the highest prevalence of UI was observed for antihistamines, where 28.4% of current users met the definition of UI. The prevalence of UI among users of tricyclic antidepressants, beta receptor agonists (indicated for asthma), and angiotensin II receptor blockers (ARBs, indicated for hypertension and heart failure) was greater than 20%. Among men, the prevalence of UI was highest among users of ARBs (22.2%), followed by loop diuretics (19.1%) and opiates/narcotics (11.6%); however, for most medications the prevalence of UI was not substantially different by user status, and was similar to the overall prevalence of UI among men.

Multivariable logistic regression models for women are shown in Table 3. For some medications, significant or near-significant associations observed in minimally-adjusted models were not robust to further covariate adjustment, suggesting those associations were confounded (i.e., aspirin, opiates, atypical antipsychotics, tricyclic antidepressants, benzodiazepines, SSRI/SNRI/serotonin modulator antidepressants, corticosteroids, and proton pump inhibitors). However, for five groups of medications, there were significant or near-significant associations with UI that remained in the parsimonious model: antihistamines (OR=1.75, 95% CI: 1.09, 2.80), beta receptor agonists (OR=1.73, 95% CI: 1.19, 2.53), ARBs (OR=2.07, 95% CI: 1.10, 3.90), anticonvulsants (OR=1.75, 95% CI: 1.00, 3.07) and estrogens (OR=1.90, 95% CI: 1.20, 3.01).

In contrast, there were fewer associations for medications and UI observed initially among men (Table 4). In parsimonious models, only anticonvulsants remained significantly associated with UI (OR=2.50, 95% CI: 1.24, 5.03). While not significantly associated with UI, ARBs were associated in the same direction and with approximately the same magnitude (OR=2.21, 95% CI: 0.96, 5.10) as in women although (as with women) the confidence interval was wide.

Discussion

We observed a higher prevalence of UI occurring at least weekly among female users of anticonvulsants, antihistamines, beta receptor agonists, ARBs, and estrogens. Nearly 3 in 10 female users of antihistamines (cyproheptadine, desloratadine, fexofenadine, or loratadine) reported weekly UI. While other medications examined based on the exploratory analysis step were not found to be associated with UI after confounder adjustment (sulfonylureas and two antiulcer classes), the association for antihistamines remained robust to confounder adjustment, but was only present among women. Most ($n=155$) were using fexofenadine ($n=76$) or loratadine ($n=70$), followed by desloratadine ($n=8$). We further examined associations with UI among women using other antihistamine classes (ethanolamines, ethylenedamines, piperazines, propylamines, and the class containing acrivastine and cetirizine) but found no significant multivariable associations. Fexofenadine and loratadine are both histamine₁ (H₁) receptor antagonists; the former is thought to cause urinary retention, which may in turn cause overflow incontinence,¹⁵ while altered micturition, urinary retention and UI are reported as adverse events for loratadine at event rates $< 2\%$.¹⁶ We were unable to find published case reports of a UI association with these medications or previous studies of subtypes of allergy medications. Given the novelty of our findings and

the popularity of these now over-the-counter medications, additional studies are needed to confirm these results. The mechanism whereby H₁ antagonists such as loratadine and fexofenadine may trigger incontinence is unclear and speculative. Activation of H₁ receptors in the urethra causes contraction; thus antagonism could relax the bladder outlet and predispose users to stress incontinence during coughing or sneezing.¹⁷ Alternatively, sneezing and coughing due to allergies raise intraabdominal pressure, which may be sufficient to lead to incontinence and our observed association may not reflect a true drug effect.

An association of similar magnitude was found for beta-2 receptor agonists, indicated for asthma. These may act directly on the smooth muscle of the bladder and urethra, which contain beta-2 receptors;¹⁸ evidence suggests such receptors are also present in the detrusor.¹⁹ It is possible that this association is confounded by coughing due to severe asthma, for which we did not have a measure in BACH; controlling for asthma had no substantial impact on the estimate, however. In a prior study, asthma medications (considered broadly) were not associated with UI in either gender.²⁰ Despite the association of angiotensin-converting enzyme (ACE) inhibitors with cough,⁵ we did not see an association for ACE inhibitors. Our findings on estrogens and UI are consistent with recent studies. In the Nurses' Health Study, oral contraceptives increased risk of incident UI among younger women,²¹ while postmenopausal hormone therapy increased risk among older women, with diminishing risk upon cessation of use.²² Similarly, in the Women's Health Initiative, conjugated estrogen preparations increased risk of UI among continent women, and worsened prevalent incontinence.²³ Ruby *et al.* also found an increased risk of UI among users of estrogens in a community-based study of older women.²⁴

The association of ARB use with UI has not, to our knowledge, previously been reported. Like H₁ agonists, angiotensin II elicits contraction of the bladder and proximal urethra. It is possible that ARBs could reduce endogenous tone of the urethra and reduce bladder outlet resistance placing subjects at risk for UI.²⁵ We had a small number of ARB users among both men and women and subsequently, imprecise CIs. It should be noted that these drugs were often used in combination with other antihypertensives in our population²⁶ suggesting more severe hypertension, so confounding by severity may be present.

Non-benzodiazepine anticonvulsants were associated with UI among both genders (albeit of borderline significance among women). This group included primidone, carbamazepine, divalproex, gabapentin, topiramate, tiagabine, oxcarbazepine, and levetiracetam; there were no significant associations in parsimonious models for benzodiazepine-type anticonvulsants. While epileptic seizures are a cause of UI, the chosen case definition of weekly UI should help circumvent 'confounding by indication', as it is unlikely that epileptic patients under drug treatment would have a seizure as often as weekly. While these anticonvulsants are used for other neurologic conditions (such as MS) and bipolar disorder, we could not identify other obvious 'confounding by indication', especially considering persons with MS were excluded. There are limited case reports of UI occurring with use of the anticonvulsants gabapentin^{27, 28} and carbamazepine.²⁹

Strengths of our study include stratification by gender (where we had distinct results), the ability to control for known UI risk factors, and the community setting. UI, as a potentially stigmatizing, embarrassing condition, may not present to medical care as often as other conditions and as such, community-based studies may be of special value. Although we did not specify all medications to be examined *a priori*, this strategy allowed for certain medications to come to attention based on an objective measure (prevalence). Further, one of the *post-hoc* identified groups (antihistamines) was robust to control for confounders in

various modeling strategies, with plausible underlying biologic mechanisms for its relationship with UI.

We removed persons with evidence of past urologic disease from our analysis, thus our results are not applicable to these individuals. A larger study in a clinical setting could help elucidate whether any potential drug effects differ in this subgroup. This cross-sectional analysis revealed associations of potential interest for further investigation, but obviously cannot determine temporal sequence or causality. Identified associations will eventually be re-examined using longitudinal data from the BACH Survey to estimate risk. Among men, fewer associations were identified, and statistical power was lower due to the lower prevalence of UI. In addition to limited power among men, we also had limited power to examine subtypes of UI among either men or women. We did not consider dose or duration of use of medications, or the effects of combinations of drugs within the same class.

Conclusions

Among women, current users of certain antihistamines, beta receptor agonists, ARBs, and estrogens had significantly higher odds of prevalent UI after multivariable adjustment. Female users of anticonvulsants had borderline higher odds of UI, while male users had significantly higher odds. These associations, some of which have not previously been identified, should be examined in longitudinal designs to determine temporality.

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TABLE 1

Demographic and medical characteristics of men and women with and without urinary incontinence (UI)*, Boston Area Community Health Survey, N=5,021.

	Women UI (N=252)	Women No UI (N=2646)	p value [†]	Men UI (N=100)	Men No UI (N=2023)	p value [†]
Mean age (SE)	53.3 (1.6)	48.1 (0.5)	<0.01	52.2 (2.2)	46.3 (0.4)	<0.01
Race/ethnicity			0.06			0.86
% Black	29.7	30.6		24.0	25.2	
% Hispanic	8.3	13.8		11.5	13.5	
% White	61.9	55.7		64.5	61.3	
Socioeconomic status			0.46			0.66
% Low	34.2	29.2		20.2	23.7	
% Middle	45.9	45.8		48.8	50.1	
% High	19.8	25.0		31.1	26.2	
% Type I or Type II diabetes	15.6	8.2	0.02	15.7	8.2	0.07
% Cardiac disease	11.2	6.0	0.06	17.6	8.2	0.08
% High cholesterol	38.1	25.5	0.01	39.3	26.7	0.07
% Stroke	0.9	0.7	0.69	2.5	1.2	0.56
% High blood pressure	41.7	24.6	<0.01	29.9	24.2	0.35
% Arthritis	53.2	24.2	<0.01	21.2	15.8	0.27
% Asthma	31.1	17.6	0.01	28.2	13.4	0.12
% Depressive symptoms	32.4	18.5	0.01	28.9	12.8	0.03
% Obese (30+ kg/m ² body mass index)	52.0	35.3	<0.01	35.9	32.4	0.62
Mean waist circumference, cm (SE)	96.0 (1.9)	89.2 (0.6)	<0.01	98.4 (2.4)	97.6 (0.7)	0.76
% Surgical menopause	18.9	13.0	0.07	--	--	--
% 1+ vaginal delivery	72.3	59.8	0.01	--	--	--
% Using medication for UI	6.2	0.6	<0.01	0.2	0.5	0.37
% Using medication for benign prostatic hyperplasia	N/A	N/A		4.0	2.8	0.51
Number of prescription medications			<0.01			0.11
% 0	22.4	38.3		34.6	51.0	
% 1-2	27.8	33.5		27.8	25.8	
% 3+	49.8	28.1		37.6	23.2	

NOTES: SE=standard error. Percents shown are column percents. Analyses weighted for sampling design.

* UI defined as urine leakage occurring weekly or more often over the past 12 months.

[‡]Overall p value for chi-square test of homogeneity.

TABLE 2

Prevalence (%) of UI* among users of 25 medication groups in the BACH Survey (N=2,898 women; N=2,123 men).

Medication	Women N users	Women Prevalence (%) of UI among users	Men N users	Men Prevalence (%) of UI among users
Antihistamines [‡]	155	28.4 [‡]	75	5.9
Autonomic				
Beta receptor agonists	238	20.9 [‡]	91	5.8
Cardiovascular Drugs				
Angiotensin II receptor blockers (ARBs)	75	22.9 [‡]	45	22.2
Angiotensin-converting enzyme (ACE) inhibitors	375	14.0	272	7.7
Beta blockers	356	12.4	236	6.0
Calcium channel blockers	238	17.8 [‡]	149	5.9
Statins	428	14.7 [‡]	290	5.8
Miscellaneous lipid lowering drugs	52	5.4	52	8.9
Central nervous system drugs				
Tricyclic antidepressants	128	20.5	53	2.8
SSRI/SNRI/serotonin modulator antidepressants	453	15.8 [‡]	202	5.0
Benzodiazepines	215	16.9	75	5.4
Anticonvulsants [§]	88	19.2	81	7.0
Atypical antipsychotics	74	16.8	57	7.7
Opiates/narcotics	184	14.6	96	11.6
COX-2 inhibitors	148	9.0	51	5.3
Carboxyl-salicylate NSAIDS	448	15.8 [‡]	402	4.1
Carboxyl-propionic NSAIDS	1222	7.8	597	3.7
Electrolytic, Caloric, and Water Balance				
Thiazide & thiazide-like diuretics	371	14.6	151	6.7
Loop diuretics	105	10.7	58	19.1 [‡]
Miscellaneous diuretics	80	18.8	27	3.9
Gastrointestinal drugs				
Histamine H2 antagonists	119	13.9	76	5.6
Proton pump inhibitors	307	20.5 [‡]	158	3.0
Hormones and synthetic substitutes				
Sulfonylurea	141	10.1	118	11.2
Synthetic corticosteroids	295	17.3 [‡]	123	5.0
Estrogens including conjugated estrogens	206	11.8	n/a	n/a

NOTES: Analyses weighted for sampling design.

* The overall prevalence of UI by our definition was 9.0% among women and 4.6% among men in our sample.

[†]This group contained only cyproheptadine, desloratadine, fexofenadine loratadine, and trimethobenzamide.

[‡]p<0.05 for chi-square test of homogeneity for UI among users vs. non-users.

[§]Includes carbamazepine, divalproex, gabapentin, levetiracetam, oxcarbazepine, primidone, tiagabine, and topiramate.

TABLE 3

Odds ratios (ORs) & 95% confidence intervals (CIs) for adjusted associations of medication groups and urinary incontinence (referent=no use) among women, N=2,898.

Medication group or class	Exposed Cases N ¹	Minimally-adjusted model ²	Parsimonious multivariable model
Antihistamines ³	29	2.47 (1.60, 3.82)	1.75 (1.09, 2.80)⁴
Beta receptor agonists	46	2.63 (1.84, 3.75)	1.73 (1.19, 2.53)⁴
Angiotensin II receptor blockers (ARBs) ⁵	18	2.35 (1.31, 4.20)	2.07 (1.10, 3.90)⁶
Angiotensin-converting enzyme (ACE) inhibitors	48	1.08 (0.74, 1.59)	
Beta Blockers	38	0.80 (0.54, 1.21)	
Calcium Channel blockers	34	1.29 (0.84, 1.98)	
Statins	57	0.92 (0.63, 1.34)	
Miscellaneous lipid lowering drugs	6	0.87 (0.37, 2.08)	
Tricyclic antidepressants	21	2.01 (1.23, 3.29)	1.42 (0.84, 2.39) ⁷
SSRI/SNRI/serotonin modulator antidepressants	68	1.95 (1.43, 2.67)	1.33 (0.95, 1.88) ⁷
Benzodiazepines	33	1.75 (1.16, 2.64)	1.09 (0.70, 1.71) ⁷
Anticonvulsants ⁸	20	2.86 (1.68, 4.88)	1.75 (1.00, 3.07) ⁴
Atypical antipsychotics	12	2.07 (1.09, 3.95)	1.33 (0.70, 2.54) ⁷
Opiates/narcotics	27	1.62 (1.05, 2.51)	0.96 (0.59, 1.54) ⁹
COX-2 inhibitors	19	1.32 (0.78, 2.24)	
Carboxyl-salicylate NSAIDS	61	1.45 (1.05, 2.00)	1.30 (0.93, 1.80) ⁹
Carboxyl-propionic NSAIDS	107	1.08 (0.82, 1.41)	
Thiazide & thiazide like diuretics	47	1.08 (0.74, 1.59)	
Loop diuretics	17	1.26 (0.71, 2.24)	
Miscellaneous diuretics	13	1.53 (0.81, 2.90)	
Histamine H2 antagonist anti-ulcer	12	1.01 (0.54, 1.90)	
Proton pump inhibitor anti-ulcer	48	1.80 (1.27, 2.57)	1.26 (0.88, 1.79) ⁹
Sulfonylurea	14	0.94 (0.52, 1.69)	
Corticosteroids	51	2.02 (1.45, 2.82)	1.39 (0.97, 1.99) ¹⁰
Estrogens including conjugated estrogens	28	1.79 (1.17, 2.75)	1.90 (1.20, 3.01)⁴

NOTES: CIs in bold exclude 1.00. Multivariable parsimonious models were built when significant or near-significant associations were observed in minimally-adjusted models.

¹ There were 252 total cases of UI among women; this column gives the number of exposed cases for each medication group.

² Minimally-adjusted model contains age (categorical) and race/ethnicity. In some analyses, the analysis population was subset on 1199 women (including 142 cases) with indications for antihypertensive medications (ARBs, ACE inhibitors, beta blockers, calcium channel blockers, and the diuretic groups) and among 1188 women (including 150 cases) with indications for lipid-lowering drugs (statins and miscellaneous lipid-lowering medications).

³ Antihistamines in this group include cyproheptadine, desloratadine, fexofenadine, loratadine, and trimethobenzamide.

⁴ Model contained beta receptor agonists, estrogens, antihistamines, and anticonvulsants and was adjusted for age (categorical), race/ethnicity, waist circumference, arthritis, and depression. Thus, medication ORs were adjusted for the effects of other medications in the model. Other covariates were considered but eliminated by the modeling strategy (see methods).

⁵ ARBs included in this group were candesartan, irbesartan, losartan, olmesartan, and valsartan.

⁶ Model adjusted for age (categorical), race/ethnicity, waist circumference, high cholesterol, asthma, arthritis, and depression.

⁷ Model contained tricyclic antidepressants, SSRIs, benzodiazepines, and atypical antipsychotics and was adjusted for age (categorical), race/ethnicity, waist circumference, arthritis, asthma, and depression. Thus, medication ORs were adjusted for the effects of other medications in the model.

⁸ Anticonvulsants included in this group were carbamazepine, divalproex, gabapentin, levetiracetam, oxcarbazepine, primidone, tiagabine, and topiramate.

⁹ Model adjusted for age (categorical), race/ethnicity, waist circumference, arthritis, asthma, surgical menopause and depression.

¹⁰ Model adjusted for age (categorical), race/ethnicity, waist circumference, arthritis, cardiac disease, asthma, and depression.

TABLE 4

Odds ratios (ORs) & 95% confidence intervals (CIs) for adjusted associations of medication groups and urinary incontinence (referent=no use) among men, N=2,123.

Medication group or class	Exposed Cases N ¹	Minimally-adjusted model ²	Parsimonious multivariable model
Antihistamines ³	6	1.69 (0.71, 4.02)	
Beta receptor agonists	6	1.20 (0.51, 2.82)	
Angiotensin II receptor blockers (ARBs) ⁴	7	2.53 (1.07, 5.96)	2.21 (0.96, 5.10) ⁵
Angiotensin-converting enzyme (ACE) inhibitors	24	2.01 (1.11, 3.61)	1.55 (0.83, 2.92) ⁵
Beta blockers	12	0.80 (0.40, 1.58)	
Calcium channel blockers	12	1.30 (0.67, 2.53)	
Statins	16	0.60 (0.31, 1.14)	
Miscellaneous lipid lowering drugs	6	2.08 (0.83, 5.23)	
SSRI/SNRI/serotonin modulator antidepressants	13	1.31 (0.71, 2.43)	
Benzodiazepines	7	1.93 (0.87, 4.29)	
Anticonvulsants ⁶	11	3.21 (1.63, 6.32)	2.50 (1.24, 5.03)⁷
Atypical antipsychotics	5	2.52 (1.00, 6.35)	1.55 (0.64, 3.78) ⁷
Opiates/narcotics	10	1.96 (0.96, 3.98)	
COX-2 inhibitors	5	1.92 (0.72, 5.12)	
Carboxyl-salicylate NSAIDS	26	1.14 (0.70, 1.86)	
Carboxyl-propionic NSAIDS	26	1.00 (0.63, 1.58)	
Thiazide & thiazide like diuretics	12	1.41 (0.70, 2.86)	
Loop diuretics	11	3.59 (1.79, 7.21)	1.82 (0.87, 3.80) ⁵
Histamine H2 antagonist anti-ulcer	5	1.27 (0.51, 3.15)	
Proton pump inhibitor anti-ulcer	14	1.61 (0.87, 2.98)	
Sulfonylurea	11	1.51 (0.76, 3.00)	
Synthetic corticosteroids	9	1.11 (0.54, 2.25)	

NOTES: CIs in bold exclude 1.00. Multivariable models were built when significant or near-significant associations were observed in minimally-adjusted models. Tricyclic antidepressants and the 'miscellaneous diuretics' group were not considered among men due to insufficient numbers for models.

¹ There were 100 total cases of UI among men; this column gives the number of exposed cases for each medication group.

² Minimally adjusted model contains age (categorical) and race/ethnicity. In some analyses, the analysis population was subset on 948 men (including 51 cases) with indications for antihypertensive medications (ARBs, ACE inhibitors, beta blockers, calcium channel blockers, and the diuretic groups) and among 844 men (including 54 cases) with indications for lipid-lowering drugs (statins and other lipid-lowering medications).

³ Antihistamines included in this group include cyproheptadine, desloratadine, fexofenadine, loratadine, and trimethobenzamide.

⁴ This medication group included users of candesartan, irbesartan, losartan, olmesartan, and valsartan.

⁵ Model adjusted for age (categorical), race/ethnicity, waist circumference, congestive heart failure, and depression. Other covariates were considered but eliminated by the modeling strategy (see methods).

⁶ Anticonvulsants included in this group: carbamazepine, divalproex, gabapentin, levetiracetam, oxcarbazepine, primidone, tiagabine, and topiramate.

⁷Model adjusted for age (categorical), race/ethnicity, waist circumference, and depression.

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