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Contribution of Common Medications to Lower Urinary Tract Symptoms in Men

While benign prostatic hyperplasia (BPH) is the most common cause, the etiology of lower urinary tract symptoms (LUTS) is multifactorial. Clinical guidelines for BPH suggest evaluating other potential sources of LUTS (eg, concomitant medication use) before initiating pharmacotherapy or surgical intervention.[1]

Through effects on detrusor muscle and urinary sphincter function, several categories of prescription drugs can worsen LUTS,[2,3] including antidepressants, antihistamines, bronchodilators, anticholinergics, and sympathomimetics.[4] By increasing urine volume, diuretics are also associated with LUTS.[5,6] Because their prevalence of use rises with patient age, prescription drugs may contribute to the age-related increase in LUTS.[7,8]

Most previous research has focused on LUTS overall, without accounting for heterogeneity in etiology. If a significant proportion of LUTS can be attributed to medication use, the observed association between a suspected risk factor and LUTS could be attenuated. Thus, it is important to determine the magnitude of the association between medications and LUTS, and the degree to which LUTS may be attributed to these medications. To this end, this study assesses the cross-sectional association between current use of selected common medications and LUTS among men enrolled in the California Men's Health Study (CMHS).

Methods. A detailed description of CMHS has been previously published.[9] Briefly, with institutional review board approval, men aged 45 to 69 years were recruited from the Kaiser Permanente California Medical Care Program (southern and northern regions). Through a 2-stage process, 84 170 participants completed questionnaires and were eligible for study inclusion using the baseline survey data and linked electronic health records between 2002 and 2003.

Men with surgery for enlarged prostate (n=1601), prostatitis (n=5547), or prostate cancer (n=5487) were excluded. Other exclusion criteria included musculoskeletal conditions (n=10 668), neurologic disorders (n=2208), and cancers including bladder and colon (n=1238). For the 63 579 remaining subjects, pharmacy records were assessed to determine prescription drug dispensation for antidepressants, antihistamines, bronchodilators, nonurinary anticholinergics, sympathomimetics, and diuretics during the baseline survey period with at least 1 prescription filled.

Severity of LUTS was assessed using the American Urological Association Symptom Index (AUASI), and additional survey data included age, race/ethnicity, and diagnosis of BPH.

Associations between drug exposures and prevalent LUTS were assessed using logistic regression models, expressed as odds ratios (ORs) with 95% confidence intervals (CIs). Primary analyses considered dichotomized AUASI, with 0 to 7 (mild) as reference vs 8 to 35 (moderate and severe), while secondary analyses stratified the latter group into moderate (8-19) and severe (≥20). Each drug category was assessed individually and collectively as a single indicator. Multivariable logistic regression models adjusted for age, race/ethnicity, region, and presence of BPH. The ORs and prevalence of drug exposures were used to estimate etiologic fraction.

Results. Baseline characteristics stratified by severity of LUTS demonstrated that older subjects displayed a progressively greater proportion of moderate to severe LUTS, with 10% of participants aged 70 to 74 years reporting severe LUTS. Asian Americans had a greater prevalence of mild LUTS, and African Americans had a greater proportion of moderate to severe LUTS.

Medication use varied by race/ethnicity ($P<.001$), with more Asian participants using antihistamines (16%) and African Americans using proportionately more diuretics (31%). Medication use increased with age ($P<.001$),

Table. Adjusted Association Between Medication Use and Lower Urinary Tract Symptoms (LUTS), Stratified by Presence of Benign Prostatic Hyperplasia (BPH), Among Participants in the California Men's Health Study

	Odds Ratio (95% CI, Wald Test)			
Medication Use	Not Adjusting for BPH, Adjusted[a]	Adjusting for BPH, Adjusted[b]	Stratified Without BPH, Adjusted[a]	Stratified With BPH, Adjusted[a]
Antihistamines	1.11 (1.06-1.17)	1.09 (1.04-1.15)	1.07 (1.01-1.13)	1.17 (1.05-1.31)
Bronchodilators	1.22 (1.15-1.29)	1.21 (1.14-1.28)	1.21 (1.13-1.29)	1.21 (1.07-1.36)
Sympathomimetics	1.10 (1.01-1.20)	1.09 (1.00-1.20)	1.13 (1.02-1.25)	0.96 (0.79-1.18)
Anticholinergics	0.96 (0.88-1.06)	0.94 (0.86-1.04)	0.92 (0.83-1.03)	1.00 (0.83-1.21)
Diuretics	1.15 (1.10-1.21)	1.19 (1.13-1.24)	1.25 (1.19-1.31)	0.98 (0.90-1.08)
Antidepressants	1.39 (1.32-1.47)	1.36 (1.29-1.44)	1.41 (1.33-1.50)	1.21 (1.07-1.35)

[a] Adjusted for age, race, region, and all medications simultaneously.
[b] Adjusted for age, race, region, benign prostatic hyperplasia, and all medications simultaneously.

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particularly for bronchodilators, anticholinergics, and diuretics, with a highest rise in diuretic use from 8% to 23% in participants aged 45 to 49 years to 70 to 74 years, respectively.

In unadjusted analyses, every medication class was associated with LUTS. When adjusted for region, age, and race/ethnicity, bronchodilators and antidepressants had the strongest associations with adjusted ORs of 1.22 and 1.39, respectively. The cohort was then stratified by presence of BPH, with 14 215 participants having BPH. Significant associations were found more often among men without BPH, particularly for sympathomimetic, diuretic, and antidepressant medications (**Table**).

When study medications were combined into any vs none, the OR was 1.29 (95% CI, 1.25-1.34) without adjustment for BPH and 1.28 (95% CI, 1.24-1.32) with adjustment for BPH. When stratified by presence of BPH, the OR was 1.31 (95% CI, 1.27-1.36) for those without BPH and 1.16 (95% CI,1.08-1.25) for those with BPH.

Estimates of etiologic fraction suggest that antihistamines, bronchodilators, diuretics, and antidepressants account for approximately 1%, 2%, 3%, and 4% of LUTS, respectively. These percentages were slightly attenuated in men with BPH. Use of any of these medications could account for 10% of LUTS, compared with 29% of symptoms associated with BPH.

Comment. This study documents the association between specific categories of common medications and LUTS in a large, diverse population of community-dwelling men. If the observed associations represent cause and effect relationships, these medications account for 10% of LUTS, an effect approximately one-third of that for BPH. This underscores the importance of assessing medications in the differential diagnosis of LUTS.

Another implication is the importance of these medications in studies of risk factors for LUTS. An outcome based solely on the presence of LUTS would include a substantial number of men with iatrogenically caused symptoms. This could dilute the association between the risk factor of interest and LUTS, obscuring a true association and leading to an incorrect conclusion that the risk factor is not associated with LUTS. In addition, the effect of these medications could explain some portion of the well-documented age-related increase in prevalence of LUTS among women that is similar in men.

The cross-sectional study design limits the ability to establish a causal relationship, and the measures of etiologic fraction represent an upper bound of the proportion of LUTS that can be attributed to these medications. There are also inherent limitations in defining medication use, since over-the-counter medications were not considered. Moreover, LUTS assessed at one discrete time may not reflect participants' typical symptom severity.

This study's significance is based on the intrinsic importance of evaluating LUTS, affecting both the research and clinical realms. Previous studies have likely underestimated these iatrogenic symptoms, leading to misclassification in observational studies of LUTS and masking of true associations that may have been amenable to intervention. Evolving treatment guidelines should consider common medication use and modify drug treatment to reduce the burden of LUTS without additional medications or invasive therapy.

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Smoking Cessation Advice Rates in US Hospitals

In 2002, The Joint Commission (TJC) and the Centers for Medicare & Medicaid Services (CMS) adopted a set of publicly reported quality measures for US hospitals that included assessment of smoking cessation advice or counseling (SCA) delivered in hospitals to smokers discharged with acute myocardial infarction (AMI), congestive heart failure (CHF), or community-acquired pneumonia (CAP).[1] The National Quality Forum is now considering a revised set of hospital-based smoking cessation measures developed by TJC for use in all hospitalized patients. The new comprehensive measures will track offers of smoking cessation medications, and they will track smoking cessation outcomes.[2] Determining the predictors of the mature SCA measure will provide insight into issues that will arise when the new SCA measures are adopted. We present the first study, to our knowledge, of patient and hospital factors associated with SCA rates using a comprehensive sample of hospitals reporting SCA data for patients hospitalized with diagnoses of AMI, CHF, and CAP.

Methods. *Data*. Patient-level data on SCA, demographic, and clinical characteristics collected under the TJC/CMS quality reporting program for 2008 were acquired from CMS.[3] The patient-level outcome was receipt of SCA, defined as hospital provision of SCA to patients with a principal diagnosis of AMI, CHF, or CAP, who were smokers at some time in the 12 months prior to admission. The hospital-level outcome was the proportion of eligible patients in a hospital who received SCA. Data on patient characteristics included age, sex, race, ethnicity, insurance coverage, length of stay, comorbidities, and discharge status. Hospital characteristics came from the 2006 American Hospital Association annual survey (numbers of beds, urban location, census region, teaching status, and ownership)[4] and by aggregating patient-level data to the hospital level.

Analyses. We tracked condition-specific SCA rates over time, modeled hospital-level SCA rates using linear regression models (excluding hospitals with <10 smokers admitted for AMI, CHF, or CAP), and estimated multilevel logistic models (for AMI, CHF, CAP, and all patients combined) with hospital random intercepts to assess factors associated with patient receipt of SCA.

Results. In 2008, nearly all patients received SCA (99% AMI [n=135 142], 97% CHF [n=131 621], and 95% CAP [n=204 504]), though SCA rates at some hospitals were still low. The mean hospital-specific SCA rates among reporting hospitals were 88% for CAP (n=4139), 91% for CHF (n=3840), and 95% for AMI (n=2813). The median hospital-specific SCA rate was 100% for smokers admitted for AMI or CHF and 98% for smokers admitted for CAP.

Predictors of Hospital-Level SCA Rates. Private-for-profit (PFP) hospitals had SCA rates 1.03 (CHF; 95% CI, 0.12 to 1.93) to 2.72 (CAP; 95% CI, 1.76 to 3.69) percentage points higher than not-for-profit (NFP) hospitals, while public hospitals had SCA rates 2.91 (CHF; 95% CI, −4.32 to −1.49) and 4.23 (CAP; 95% CI, −5.63 to −2.82) percentage points lower than NFP hospitals. Hospitals where a minimum of 9% of patients with AMI or CHF were Medicaid recipients had SCA rates 0.92 (AMI; 95% CI, −1.44 to −0.40) and 1.09 (CHF; 95% CI, −1.79 to −0.39) percentage points lower than hospitals with fewer Medicaid patients in these diagnosis categories.

Predictors of Smoking Cessation Advice Receipt. The **Table** presents predictors of individual patient receipt of SCA. Indicators of patient frailty (age and discharge status) were associated with lower SCA rates; patients discharged to an institution had at least 75% lower odds of receiving SCA than patients discharged home across all 3 diagnoses. Minority and Medicaid patients were generally less likely to receive SCA. Hospital-level factors including ownership type and proportion of patients on Medicaid also predicted individual receipt of SCA.

Comment. Near-universal provision of SCA in 2008 is in stark contrast to the level of SCA reported in 2002, the first year of public reporting, where the mean SCA rate at US hospitals was 67% for AMI, 42% for HF, and 37% for CAP.[5] While the current high rates of SCA provision are positive steps, from a public health perspective, it is not clear that our findings necessarily reflect the delivery of effective smoking cessation interventions due to limitations inherent in the current SCA measure and the limited form of SCA it assesses.[6,7] Despite very high levels of documentation of SCA provision, differences persist across hospitals and patients nationally. Particularly troubling is the evidence that SCA rates fall short for frail and minority patients as well as hospitals serving vulnerable populations.

Forthcoming updates to the SCA measures are closely tied to the smoking cessation evidence base and have real potential to improve cessation rates and health outcomes for hospitalized smokers given hospitals' high motivation to improve quality on publicly reported measures tied to pay-for-participation incentives. Nevertheless, our findings of persistently lower SCA rates in some vulnerable populations hint at a strong possibility that disparities will continue in the new smoking cessation measures, potentially becoming exacerbated in the context of their more stringent demands.

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