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Sex disparities in diagnosis of bladder cancer after initial presentation with hematuria: a nationwide claims-based investigation

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Abstract

Background—Women have disproportionately higher mortality rates relative to incidence for bladder cancer. Multiple etiologies have been proposed, including delayed diagnosis and treatment. Guidelines recommend rule-out of malignancy in men and women presenting with hematuria. We aimed to determine the difference in timing from presentation with hematuria to diagnosis of bladder cancer in women versus men.

Methods—This is a retrospective population-based study examining the timing from presentation with hematuria to diagnosis of bladder cancer, based on data from the MarketScan databases, which include enrollees of more than 100 health insurances plans of approximately 40 large US employers from 2004 through 2010. All study patients presented with hematuria and were subsequently diagnosed with bladder cancer. The primary outcome measure was number of days between initial presentation with hematuria and diagnosis of bladder cancer by gender.

Results—5416 men and 2233 women met inclusion criteria. Mean days from initial hematuria claim to bladder cancer claim was significantly longer in women (85.4 vs. 73.6 days, $p<0.001$), and the proportion of women with >6 month delays in bladder cancer diagnosis significantly higher (17.3% vs. 14.1%, $p<0.001$). Women were more likely to be diagnosed with urinary tract infection (OR 2.32 [95% CI 2.07–2.59]) and less likely to undergo abdominal or pelvic imaging (OR 0.80 [95% CI 0.71–0.89]).

Conclusions—Both men and women experience significant delays between presentation with hematuria and diagnosis of bladder cancer, with longer delays for women. This may be partly responsible for the gender-based discrepancy in outcomes associated with bladder cancer.

MeSH Keywords

Urinary Bladder Neoplasms; Hematuria; Diagnosis; Insurance Claim Review; Standards

There were an estimated 73,510 incident cases of bladder cancer in the United States in 2012, with 55,600 and 17,910 cases in males and females, respectively (3.1 to 1 ratio).[1,2] Of

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the 14,880 estimated deaths from bladder cancer, 10,510 were men and 4,370 women (2.4 to 1 ratio),[2] demonstrating the disproportionate mortality:incidence ratio for women that is well-documented in the literature.[3–7] Specifically, a study by the EUROCARE Working Group[8] demonstrated a 5% absolute decreased 5-year survival for women compared to men, controlling for age and expected mortality. This phenomenon was unique to bladder cancer, as the EUROCARE study found that women appeared to have a significant survival advantage for cancers of the head and neck, esophagus, stomach, liver, and pancreas.

The mechanisms for increased mortality in women with bladder cancer are not completely understood. Although advanced stage of presentation has been hypothesized, a review of the SEER database by Mungan *et al*. demonstrated a 5-year overall relative survival advantage for males across all stages of disease.[5] Studies evaluating disparities in aggressive treatment are mixed and do not appear to explain the disparity in prognosis,[9,10] nor does in-hospital mortality following aggressive therapy.[11] However, for both men and women, it has been established that delays in diagnosis and treatment (specifically, a delay >6 months for diagnosis[12] and >12 weeks from diagnosis to cystectomy[13–16]) adversely impact survival. Furthermore, recent studies suggest that relative to men, women may be at greater risk of delays in diagnosis[17] and presentation with advanced disease.[18]

Gross hematuria is the most prognostic clinical sign of underlying urologic malignancy, with urothelial cell carcinoma present in 13% to 34.5% of cases.[19,20] Microscopic hematuria is associated with malignancy in 0.5% to 10.5% of cases.[20–23] As such, even in cases of asymptomatic microscopic hematuria, the American Urological Association Guidelines recommend a thorough work-up for malignancy, consisting of upper tract imaging and cystoscopy, following rule-out of obvious benign causes.[24] In patients 40–59 years of age, gross hematuria carries a positive predictive value (PPV) for urologic cancer that is actually higher for women than men (6.4% vs. 3.6%).[25] Nonetheless, women presenting with hematuria are less likely to see a urologist, with one study demonstrating men to be 65% more likely to receive a urologic referral.[26] This is thought to be related to the differential assumption of a benign diagnosis in women.[27] A recent study of patients ultimately diagnosed with bladder cancer found women to be less likely to have undergone prompt urologic consultation for their presenting symptoms and were more likely to have received 3 or more courses of antibiotics.[28]

If women are more likely to die from bladder cancer than men at any stage as the literature suggests,[8] and that delay in diagnosis and treatment adversely impacts survival,[12,14–16] timely diagnosis of bladder cancer in women is of utmost importance. Our study aims to evaluate gender disparities in the timing from clinical presentation with hematuria to the diagnosis of bladder cancer in a large nationwide cohort.

METHODS

Data Source

Data were obtained from the Thomson Reuters MarketScan Commercial Claims and Encounters Database,[29] which has collected longitudinally-linked claims data on approximately 40 self-insured employers since 1994. MarketScan data extraction has been particularly robust since 2004, and by 2010, the databases contained claims data linking episodes of care on 40 million patients. The MarketScan databases contain information on patient demographics, dates of service, *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) diagnostic codes, *Current Procedural Terminology* (*CPT*) codes, and other data. As a limited dataset with no identifiable personal health information, MarketScan analysis is exempt from Institutional Board Review, and exempt-status was confirmed by our institution's IRB prior to initiating the study.

Data collected on each patient focused on our primary outcome measure, which was number of days between initial hematuria claim and initial bladder cancer claim. Secondary outcome analysis evaluated the proportion of patients with extended delay from initial hematuria claim to initial bladder cancer claim, timing and number of hematuria visits, diagnosis of UTI, number of courses of antibiotics, and receipt of upper tract imaging and cytology. Over the course of the study period, there was a gradual incorporation of expanded hematuria ICD-9 codes in clinical practice (i.e. unspecified, gross, and microscopic), and the ICD-9 hematuria claim billed for each patient's initial hematuria visit was also extracted. Specific ICD-9 and CPT codes are provided in Table 1.

Study Population

We queried the MarketScan outpatient care databases to identify those patients who had an initial bladder cancer claim between 2004 and 2010. Only those patients who had an initial hematuria claim within 12 months of their initial bladder cancer claim were included in the study population. We chose a window of one year to limit potential cases where the initial hematuria claim may not be related to the incident bladder cancer, as might, for example, be observed with a two year window. Patients were additionally required to have been present within the MarketScan databases for two years prior to their initial hematuria claim without claims for bladder cancer or hematuria within this precedent period.

Data Analysis

Baseline demographic data for men and women were summarized using standard descriptive statistics (means and standard deviation or 95% confidence intervals and/or medians and interquartile ranges for continuous variables; sample sizes and proportions for categorical variables). Student's t-test or Mann-Whitney U-test was performed for comparison of continuous variables and chi-square test for comparison of categorical variables.

Subset analysis of days to bladder cancer claim was performed based on the ICD-9 billing code claimed at each patient's initial hematuria visit. This was planned *a priori*, based on the hypothesis that, for example, gross and microscopic hematuria might receive differential work-up in clinical practice. Univariate logistic regression analysis was performed to assess odds of >3 month, >6 month, and >9 month delay from initial hematuria claim to initial bladder cancer claim based on multiple clinical and demographic factors. These time intervals for "extended delay" were chosen to model previous studies demonstrating the clinical significance of 3 month intervals in delay in diagnosis[12] and treatment.[13–16] Multivariable logistic regression analysis was performed to assess the impact of gender on odds of delay in diagnosis of 3, 6, and 9 months, adjusted for those variables found to be clinically and statistically significant based on univariate analysis. Multivariate linear regression was used to perform adjusted analysis of the delay between presentation with hematuria and diagnosis of bladder cancer as a continuous variable. Charlson Comorbidity Index (CCI) scores were calculated using the Healthcare Cost and Utilization Project (HCUP-US) software, which assigns variables that identify comorbidities in medical records using ICD-9 codes [Comorbidity Software, Version 3.7].

All analyses were performed with Stata, version 12.0, statistical software (StataCorp, College Station, TX). A two-sided p-value <0.05 was considered statistically significant.

RESULTS

There were 7649 patients who met inclusion criteria, of whom 5416 were men and 2233 were women. Patient characteristics are highlighted in Table 2. Women on average were significantly younger (mean age 55.7 ± 7.8 vs. 57.0 ± 7.2 years, $p<0.001$) and less comorbid

(mean CCI 0.46 ± 0.84 vs. 0.52 ± 0.91, p=0.004). While there was no evidence of a difference between men and women in proportion with initial ICD-9 claim for unspecified hematuria, women were significantly more likely to have an ICD-9 claim for microscopic hematuria (p<0.001) and less likely to have an ICD-9 claim for gross hematuria (p=0.02). There was no difference in the mean number of hematuria visits prior to the diagnosis of bladder cancer between men and women (mean number of visits 2.74 for both men and women, p=0.46).

The delay between initial hematuria claim and bladder cancer diagnosis was significantly longer for women (mean 85.4 ± 97.7 vs. 73.6 ± 91.1 days, p<0.001). Additionally, women were significantly more likely to have experienced delays of greater than 3 months, 6 months, and 9 months between hematuria presentation and bladder cancer diagnosis (30.9% vs. 24.5%, p<0.001; 17.3% vs. 14.1%, p<0.001; and 9.4% vs. 7.1%, p=0.001, respectively) (Table 3). Women underwent significantly more urinalyses (mean per patient 1.39 ± 1.61 vs. 1.19 ± 1.35, p<0.001) and urine cultures (mean per patient 0.83 ± 1.20 vs. 0.53 ± 0.86, p<0.001) and were significantly more likely to receive antibiotics (40.1% vs. 35.4%, p<0.001). Women were more likely to be diagnosed with urinary tract infection (33.1% vs. 17.6%, OR 2.32 [95% CI 2.07–2.59], p<0.001), and 8.7% of women underwent 3 or more courses of antibiotics prior to diagnosis of bladder cancer as compared to 5.2% of men (p<0.001). In contrast, women were less likely than men to undergo upper tract imaging (73.1% vs. 77.3%, OR 0.80 [95% CI 0.71–0.89], p<0.001) (Table 3).

Subgroup and Regression Analysis

Among those patients with initial ICD-9 hematuria claim of unspecified hematuria women experienced greater delays in time to diagnosis of bladder cancer (89.8 ± 99.7 vs. 76.5 ± 92.9 days, p<0.001) and were more likely to have delays of 3 to 6 months, 6 to 9 months, and 9 to 12 months (p<0.001) (Table 4). The data did not support a difference in either measure among those patients with initial ICD-9 hematuria claim of gross or microscopic hematuria.

Univariate regression analysis assessing odds of >3 month, >6 month, and >9 month delay between presentation with hematuria and diagnosis of bladder cancer is summarized in Table 5. Across all time categories, gross hematuria predicted for decreased odds of an extended delay between presentation and diagnosis. In contrast, female gender, increasing CCI, increasing number of hematuria visits, and diagnosis of UTI were associated with a significantly increased likelihood of a delay in diagnosis of >3, 6, and 9 months. Metropolitan statistical area and region of the country did not significantly predict for a delay of any length. There was no clear pattern indicating the influence of year of visit on odds of extended delay.

Female gender remained a significant predictor of >3 month, >6 month, and >9 month delay between hematuria claim and bladder cancer diagnosis (OR 1.26 [95% CI 1.12–1.42], OR 1.16 [95% CI 1.00–1.33], and 1.23 [95% CI 1.02–1.48], respectively) on multivariable regression analysis adjusted for age, UTI claim, number of hematuria visits, CCI, hematuria ICD-9 code, and year of diagnosis (Table 5). Gross hematuria remained the most protective variable against an extended delay (OR 0.46 [95% CI 0.36–0.58], OR 0.51 [95% CI 0.38–0.69], and OR 0.56 [95% CI 0.38–0.84] for >3, 6 and 9 months, respectively) whereas a UTI claim conferred the greatest odds of an extended delay (OR 1.97 [95% CI 1.74–2.22], OR 1.92 [95% CI 1.66–2.21], OR 1.79 [1.49–2.16] for >3, 6 and 9 months, respectively). On adjusted linear regression analysis, female gender predicted for a 7.3 day additional delay (95% CI 2.9 to 11.7 days), and presence of a UTI claim was associated with an additional delay of 27.9 days (95% CI 23.0–32.7 days).

DISCUSSION

This study evaluates gender-based differences in timing and clinical course from presentation with hematuria to diagnosis of bladder cancer. Our analysis of a large privately insured population suggests that on average the delay between presentation with hematuria and diagnosis is nearly 2 weeks longer for women than for men. In addition, women are over 15% more likely than men to experience a delay in diagnosis of greater than 6 months and approximately 25% more likely to experience a delay of greater than 9 months. The results of our study are most concerning on two levels. First, given the well-described inferior survival outcomes for women with bladder cancer,[3–6,8] and the impact of delayed diagnosis on survival,[12] prompt diagnosis of bladder cancer in women is exceedingly important. Second, while the data suggests we are disproportionately failing to avoid significant delays in diagnosis in women, approximately 1 in 7 men are also experiencing delays greater than 6 months in diagnosis of bladder cancer.

The clinical sign of hematuria is not trivial, with up to one-third of patients with gross hematuria and a tenth of those with microscopic hematuria harboring bladder cancer.[19–23] Furthermore, while most patients have non-invasive urothelial cell carcinoma at diagnosis, up to 50% will have high grade disease.[30] The 2012 American Urological Association (AUA) guidelines on the evaluation of asymptomatic microscopic hematuria in adults recommend cystoscopy in all patients over 35 years of age and upper tract imaging in those without an obvious benign cause of hematuria.[24] Urinary cytology should be considered for those with persistent microhematuria after negative workup or those with risk factors for *carcinoma in situ* including irritative voiding symptoms and history of tobacco use or chemical exposure.

In Hollenbeck *et al.*'s review of the linked Surveillance, Epidemiology, and End Results-Medicare database, a delay in diagnosis of bladder cancer from diagnosis of hematuria of 6 to 9 months and greater than 9 months resulted in a cancer-specific mortality hazard ratio of 1.19 [95% CI 1.11–1.28] and 1.29 [95% CI 1.14–1.45], respectively, when adjusted for stage and grade.[12] Herein, within a younger cohort, we noted that 7.8% of patients will experience a delay greater than 9 months (9.4% in women vs. 7.1% in men). Interestingly, Hollenbeck *et al.* noted the strongest effect of delay on cancer-specific mortality was observed among those with low grade (HR 2.11 [95% CI 1.69–2.64]) and low stage disease (HR 2.02 [95% CI 1.54–2.64]). Thus, although the MarketScan database does not contain pathologic stage and grade information, it appears that a delay in diagnosis may remain relevant to cancer-specific survival even for the lowest risk patients.

In contrast to the study of Medicare beneficiaries by Hollenbeck and colleagues, our analysis of the MarketScan Database evaluates a population of privately-insured individuals <65 years of age. Across periods of delay, we identified only a very modest protective effect of age that maintained significance on adjusted analysis only against delay greater than 3 months (but not >6 or >9 months). Furthermore, Lyratzopoulous *et al.*, whose study contained men and women of any age, did not identify age as a significant predictor of delayed diagnosis.[17] Although this would suggest that the gender disparity observed within our younger study population would apply to an older population in which cancer is more common, further study in a larger cohort of older patients may be required.

The reasons for delay are likely multifactorial. Johnson and colleagues found in a claims-based study that only 47% of 559 men and 28% of 367 women presenting with hematuria were referred for urologic evaluation.[26] Similarly, Lyratzopoulous *et al.* demonstrated that women ultimately diagnosed with bladder cancer were 2.29 (95% CI 1.97–2.67) times as likely to undergo three or more primary care visits for hematuria prior to urologic referral,[17]

while Nieder *et al*. found that only a fraction of primary care physicians routinely refer patients to urology for hematuria.[27] Our data would suggest that prolonged work-up and treatment of UTI over multiple visits for hematuria underlies the delay in cancer diagnosis and disparately impacts women: a UTI billing claim was the single strongest independent predictor of delay in diagnosis of bladder cancer after initially presenting with hematuria (approximately doubled risk of extended delay), and women were significantly more likely to have a UTI claim (OR 2.3). Henning *et al.* documented a similar predilection towards work-up and treatment of UTI in a multi-institutional study in which patients presenting for transurethral resection of bladder tumor were surveyed regarding their pre-diagnosis clinical course.[28] In addition to referral patterns, patient beliefs and compliance as well as access to care may also play a significant role in delayed diagnosis but have received limited study.

The reasons for the relatively modest differences in delay between men and women (mean difference 12 days, adjusted increased odds of 15–25% across all time periods) are likely multifactorial. First, while female gender conferred a risk of increased time from hematuria to diagnosis of bladder cancer, the mean time to diagnosis for men remained lengthy at 73.6 days. Therefore the relative difference in delay is less pronounced. In addition, our study population is inclusive only of insured patients. It is possible that disparities would be more extensive in patients with poorer access to care.[18]

The focus of this study is delay in diagnosis, however, it is worthwhile to note that delays between diagnosis of bladder cancer and treatment have also been associated with increased mortality rates. Several papers have shown that patients experiencing delays >12 weeks between diagnosis of muscle-invasive disease and radical cystectomy have increased mortality (HR 1.6–2.1)[13,14,16] and worse pathologic outcomes (81–84% with extravesical or nodal disease vs. 48–52% organ-confined).[13,15]

Our study has several limitations that deserve mention. Weaknesses of the MarketScan database are similar to that of other administrative databases, including errors of omission in claims, inability to collect important data on risk factors (e.g. smoking history), and no data on outcomes such as bladder cancer stage and survival. In addition, MarketScan covers only insured patients (who have the highest access to care) and therefore may underestimate the delay between presentation with hematuria and diagnosis of bladder across all U.S. patients. Lastly, MarketScan databases do not include patients over 65 years of age. Although the guidelines clearly state that younger patients also merit a urological evaluation, increased age was associated with decreased risk of a greater than 3 month delay in diagnosis in our study. It is unclear to what extent the gender-based disparity in delay described herein would translate to an otherwise comparable but older study population.

Our investigation represents the first to quantify timing between presentation of hematuria and diagnosis of bladder cancer and the gender-specific clinical courses incurred during this delay. In our nationwide sample, approximately 1 in 6 women and 1 in 7 men were diagnosed with bladder cancer greater than 6 months from initial presentation with hematuria. This highlights a problem for all patients, and may prove a contributing factor for women's relatively adverse survival outcomes. Improved education and adherence to guidelines could greatly benefit our future patients.

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Table 1

International Classification of Dieases, Ninth Revision, Clinical Modification (*ICD-9-CM*) diagnostic codes and *Current Procedural Terminology* (*CPT*) codes used in data extraction

Diagnosis or Diagnostic Test	ICD-9 or CPT Codes
Malignant neoplasm of urinary bladder	188, 188.1–188.9, 233.7
Hematuria	599.7, 599.70, 599.71, 599.72
Urinary tract infection	599.0
Imaging	
CT abdomen and/or pelvis	74150, 74160, 74170, 72192, 72193, 72194
Ultrasound	76770, 76775, 76857
Intravenous pyelography	74400, 74410, 74415
Urinalysis	81001, 81002, 81003, 81005, 81007, 81015, 81020
Urine culture	87086, 87088, 87184, 87186
Urine cytology	88104, 88108, 88112
Cystoscopy	52000, 52005, 52204, 52281, 52224

Table 2

Baseline patient characteristics.

	Men (N=5416)	Women (N=2233)	P-value
Age, years (95% CI)	57.0 (56.8–57.2)	55.7 (55.4–56.1)	<0.001
Charlson Comorbidity Index score (95% CI)	0.52 (0.50–0.55)	0.46 (0.43–0.50)	0.004
From metropolitan statistical area	81.5%	83.9%	0.01
Number of hematuria visits (95% CI)	2.74 (2.70–2.79)	2.74 (2.67–2.81)	0.46
Hematuria ICD-9 code			
Hematuria unspecified	85.8%	85.1%	0.41
Gross hematuria	9.2%	7.5%	0.02
Microscopic hematuria	5.0%	7.4%	<0.001

Table 3

Assessment of clinical course from initial hematuria presentation to diagnosis with bladder cancer.

	Men	Women	P-value
Delay in diagnosis of bladder cancer from presentation with hematuria			
Mean no. days from hematuria presentation to bladder cancer diagnosis (95% CI)	73.6 (71.2–76.1)	85.4 (81.3–89.4)	<0.001
Median no. days from hematuria presentation to bladder cancer diagnosis (IQR)	35 (15, 88.5)	41 (17, 117)	<0.001
Delay < 3 months, n (%)	4068 (75.1)	1538 (68.9)	<0.001
Delay 3 to 6 months, n (%)	583 (10.8)	308 (13.8)	
Delay 6 to 9 months, n (%)	379 (7.0)	177 (7.9)	
Delay 9 to 12 months, n (%)	386 (7.1)	210 (9.4)	
Infectious work-up			
Urinalysis sent	65.8%	67.8%	0.11
Mean no. of urinalyses sent (95% CI)	1.19 (1.16–1.45)	1.39 (1.16–1.23)	<0.001
Urine culture sent	38.5%	49.8%	<0.001
Mean no. of urine cultures sent (95% CI)	0.53 (0.51–0.55)	0.83 (0.78–0.88)	<0.001
UTI claim present	17.6%	33.1%	<0.001
Any antibiotic filled	35.4%	40.1%	<0.001
Malignant work-up			
Any abdominal/pelvic imaging	77.3%	73.1%	<0.001
Cytology sent	36.0%	39.0%	0.01

Table 4

Analysis of delay in diagnosis by hematuria ICD-9 code

Hematuria ICD-9 Code	Men N (%)	Women N (%)	P-value
Unspecified	**4648 (71.0)**	**1900 (29.0)**	**<0.001**
Delay < 3 months, %	73.9	66.8	<0.001
Delay 3 to 6 months, %	11.1	14.6	
Delay 6 to 9 months, %	7.4	8.4	
Delay 9 to 12 months, %	7.6	10.1	
Gross	**498 (74.8)**	**168 (25.2)**	**0.43**
Delay < 3 months, %	86.6	83.9	0.56
Delay 3 to 6 months, %	5.6	7.7	
Delay 6 to 9 months, %	4.0	3.0	
Delay 9 to 12 months, %	3.8	5.4	
Microscopic	**270 (62.1)**	**165 (37.9)**	**0.80**
Delay < 3 months, %	74.4	77.0	0.53
Delay 3 to 6 months, %	14.4	10.3	
Delay 6 to 9 months, %	5.2	7.3	
Delay 9 to 12 months, %	5.9	5.5	

Table 5

Regression analysis assessing odds of increased delay between initial hematuria presentation and diagnosis of bladder cancer.

	Univariate*		Multivariate**	
Variable	**OR**	**95% CI**	**OR**	**95% CI**
Delay >3 months				
Age	0.992	0.985–0.999	0.990	0.983–.0997
Female gender	1.38	1.23–1.54	1.26	1.12–1.42
UTI claim	2.41	2.15–2.71	1.97	1.74–2.22
No. of hematuria visits	1.44	1.39–1.48	1.41	1.36–1.45
CCI	1.14	1.08–1.20	1.14	1.07–1.21
Hematuria ICD-9				
Unspecified (reference)	-	-	-	-
Gross	0.41	0.33–0.52	0.46	0.36–0.58
Microscopic	0.80	0.64–1.01	0.97	0.76–1.23
Delay >6 months				
Age	0.998	0.990–1.005	0.996	0.988–1.005
Female Gender	1.27	1.11–1.45	1.16	1.00–1.33
UTI claim	2.32	2.03–2.66	1.92	1.66–2.21
No. of hematuria visits	1.33	1.29–1.38	1.29	1.25–1.34
CCI	1.13	1.06–1.21	1.11	1.03–1.19
Hematuria ICD-9				
Unspecified (reference)	-	-	-	-
Gross	0.46	0.34–0.61	0.51	0.38–0.69
Microscopic	0.68	0.51–0.93	0.82	0.60–1.11
Delay >9 months				
Age	0.999	0.988–1.010	0.998	0.987–1.010
Female gender	1.35	1.13–1.61	1.23	1.02–1.48
UTI claim	2.22	1.86–2.65	1.79	1.49–2.16
No. of hematuria visits	1.30	1.25–1.36	1.26	1.21–1.32
CCI	1.10	1.01–1.20	1.06	0.97–1.17
Hematuria ICD-9				
Unspecified (reference)	-	-	-	-
Gross	0.49	0.33–0.73	0.56	0.38–0.84
Microscopic	0.68	0.45–1.03	0.81	0.53–1.23

Abbreviations: UTI, urinary tract infection; CCI, Charlson Comorbidity Index score; MSA, metropolitan statistical area

* Metropolitan statistical area, geographical region, and year of hematuria diagnosis also evaluated. No significant association.

** Year of hematuria diagnosis also included in multivariate analysis to account for temporal changes in ICD-9 coding