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Incidence and management of uncomplicated recurrent urinary tract infections in a national sample of women in the United States

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Abstract

Objective—To determine the incidence and characteristics of women with uncomplicated recurrent UTIs and to explore whether the use of culture-driven treatment affects rates of UTI-related complications and resource utilization.

Methods—Using MarketScan claims from 2003 to 2011, we identified UTI naive women ages 18–64 with incident uncomplicated recurrent UTIs. Recurrent UTIs were defined as 3 UTI visits associated with antibiotics during a 12-month period. Cases were excluded if they had a UTI in the preceding year, or if they had any complicating factors (e.g. abnormality of the urinary tract, neurologic condition, pregnancy, diabetes, or currently taking immunosuppression). We next assessed use of urine cultures, imaging, and cystoscopy and performed propensity score matching with logistic regression to determine whether having a urine culture associated with >50% of UTIs affected rates of complications and downstream resource utilization.

Results—We identified 48,283 women with incident uncomplicated recurrent UTIs, accounting for an overall incidence of 102 per 100,000 women, highest among women ages 18–34 and 55–64. 61% of these women had at least 1 urine culture, 6.9% had imaging, and 2.8% had cystoscopy. Having a urine culture >50% of the time was associated with fewer UTI-related hospitalizations and lower rates of IV antibiotic use, while demonstrating higher rates of UTI-related office visits and pyelonephritis.

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Conclusions—The incidence of uncomplicated recurrent UTIs increases with age. Urine culture directed care is beneficial in reducing high cost services including UTI related hospitalizations and IV antibiotic use, making them a valuable component to management of these patients.

Keywords

Epidemiology; cystoscopy; urine culture; imaging; propensity score analysis

Introduction

Urinary tract infections (UTIs) are the most common type of bacterial infection,[1] accounting for enormous morbidity and mortality on both an individual and societal level. Prior research from the Urologic Diseases in America Project estimated the overall lifetime prevalence of UTI in women to be over 50%,[2] accounting for over $2.6 billion in annual costs in the United States alone.[3]

Within this population exists a subgroup of women who get recurrent urinary tract infections, defined as 3 or more culture proven infections within a 12 month period, or as 2 or more culture proven infections in a 6 month period.[4] These infections are further classified as uncomplicated if they occur in healthy individuals who have no structural or functional abnormalities.[5] European and Canadian guidelines for treatment of uncomplicated recurrent UTIs both recommend diagnosis by urine culture and discourage the use of either cystoscopy or imaging.[6,7] However, information on the epidemiology and management of uncomplicated recurrent UTIs in women are lacking.

To address these deficits in our understanding of this important and costly condition, we designed a cohort study using national MarketScan claims from 2003 to 2011. Our primary objective was to determine the incidence and to further characterize this population of women with uncomplicated recurrent UTIs. Our secondary aim was to explore whether culture-directed therapy for uncomplicated recurrent UTIs is associated with decreased downstream utilization of resources. Findings from this study will highlight important epidemiologic and clinical factors associated with this condition with the goal of informing future treatment guidelines and strategies in these patients.

Materials and Methods

Database; MarketScan

This is a cohort study of women with incident uncomplicated recurrent UTIs using MarketScan data from 2003 to 2011. MarketScan includes de-identified employer-based healthcare claims from approximately 150 payers in the United States on over 66 million lives. These data represent a nationally representative sample of Americans and include information on individual-level health (medical and drug), laboratory results, and hospital discharges.[8]

Definition of incident cases of uncomplicated recurrent UTIs

The study population was comprised of women ages 18 to 64 with incident recurrent uncomplicated UTIs. To define incident cases of recurrent UTIs, the study period for each subject began 1 year after entry into the dataset without any UTIs. Once this specification was met, we identified the first UTI for each subject, referred to as the index UTI. Each subject was then followed longitudinally for subsequent UTIs over the next 12 months (referred to as the definitional period). The presence of a 3rd UTI during this time period qualified the subject as a case. If the subject did not have 3 UTIs during this time period, the process started over with subsequent UTIs until either the definitional criteria were met or the patient was excluded as a case.

For the purposes of this study, a UTI was defined as an evaluation and management visit (either in the office, outpatient clinic, or emergency room setting) associated with a diagnosis for urinary tract infection based on *International Classification of Diseases, Ninth Revision (ICD-9) codes* (Supplement) with administration of antibiotics within a 14 day window of the date of that visit, similar to methods previously described in the literature.[9] We chose a 14-day window for antibiotics prescriptions associated with the UTI visit was chosen to allow for delays in claims processing. Antibiotic prescriptions for urinary tract infections were limited to those with less than 30 days supply to exclude prescriptions for antibiotic prophylaxis.[9]

In order to identify uncomplicated (versus complicated) UTIs, we excluded women with urinary tract stones, ureteral abnormalities/vesicoureteral reflux, neurologic conditions, pregnancy, and diabetes (Supplement) based on ICD-9 codes present during the 12 -month definitional period and the year preceding this time period.

Additional Measures

Summary measures of the study cohort were obtained from MarketScan claims based on ICD-9 codes from the year prior to the definitional period (Supplement). Characteristics included subject age, geographic region, insurance, comorbidity and the presence of clinical characteristics that may influence UTIs (e.g. pelvic organ prolapse, urinary incontinence, and being on antibiotic prophylaxis). Comorbidity was calculated using established methods described by Klabunde.[10]

Insurance was classified into the following 5 categories based on coverage characteristics: (1) preferred provider organization (PPO), (2) comprehensive, (3) exclusive provider organization and health maintenance organization (EPO/HMO), (4) point-of-service (POS), and (5) deductible health plan (DHP). In PPOs, patients are incentivized to seek care within their network, but can seek care outside of their network if requested. A primary care physician (PCP) is not required and specialist referrals are not necessary. In the comprehensive plan, the patient can use any provider and there is only one policy. In the EPO/HMO group, patients are incentivized to use certain providers and must have a PCP and specialty referrals. POS care differs from the EPO/HMO group in that out of network services are covered and payments are fully or partially capitated. Finally, in the DHP group, patients do not need to have PCPs, referrals to specialists, and payments are not capitated.

To calculate incidence of women with uncomplicated recurrent UTIs, the numerator was defined based on the definition provided above (3 UTI related visits associated with a prescription for antibiotics in a 12 month period) and the denominator included all women ages 18–64 in the MarketScan claims data during the study period. Of note, the denominator required that women had a 1 year eligibility period prior to the definitional UTI period, but did not require an additional 1 year of eligibility after the definitional period, making the denominator used to calculate recurrent UTI incidence greater than that used in other analyses in this manuscript.

In order to understand resource utilization during the incident UTI period, we evaluated frequencies of urine culture, cystoscopy, and imaging [X-ray, CT scan, magnetic resonance imaging (MRI), and urologic imaging] based on Current Procedure Terminology Codes (CPT-4), (Supplement).

Next, to better understand downstream resource utilization, we explored the use of imaging, cystoscopy, UTI related emergency room, inpatient, and clinic visits, use of IV antibiotics associated with UTIs, and frequency of pyelonephritis in the year following the definitional period.

Statistical Analysis

Descriptive characteristics are presented as frequencies and percentages. Incidence of uncomplicated recurrent UTIs, both overall and stratified by age group, were calculated using the definition described above as the numerator and the number of eligible women with claims in MarketScan data as the denominator.

In order to determine whether women with uncomplicated recurrent UTIs (3 UTIs in 12 months) differed from women with uncomplicated non-recurrent UTIs (1 or 2 UTIs in 12 months), we compared baseline patient characteristics between women with 1, 2 and 3 UTIs in a 12-month period.

To examine the association between urine culture orders and resource utilization, we categorized the sample according to whether or not urine cultures were obtained during more than 50% of the UTI episodes (at least 2/3 UTIs). We estimated the propensity of obtaining a urine culture during more than 50% of the episodes using a logistic regression conditional on patient age, comorbidity, Charlson score, continence status, presence of pelvic organ prolapse, antibiotic prophylaxis, geographic region, and insurance status and used it to match patients with a urine culture during more than 50% of episodes to the ones with it under less than 50% of episodes (a nearest neighbor algorithm was used for the matching). Conditional on the propensity score estimate, patients are likely to have or have not done urine culture by chance and as such one-to-one matching of patients with and without urine culture that have similar propensity score provide a non-parametric way to control for selection bias. We used the doubly robust[11] method where in addition to the propensity score matching, we conducted a multivariate regression on the matched sample to assess the association between urine cultures and the following outcomes: emergency room visits, office visits, inpatient visits, use of IV antibiotics, and occurrence of pyelonephritis. All analyses were performed using SAS 9.2 Software.

Results

We identified 48,283 women with incident uncomplicated recurrent UTIs out of a denominator of 47,337,422 women from 2004 to 2010 using MarketScan data. We then determined the overall incidence of uncomplicated recurrent UTIs to be 102 cases per 100,000 women. Incidence represented a "J" shape distribution based on age, with a rate of 105/100,000 women ages 18–34, 76 and 77/100,000 women ages 35–44 and 45–54 (respectively), and 189/100,000 women ages 55–64 (Figure 1). A total of 28,545 women with uncomplicated recurrent UTIs met our eligibility criteria in the year following the UTI definitional period and were included in the remainder of the analyses.

Baseline characteristics differed between the 28,545 women who met our definitional criteria of uncomplicated recurrent UTIs (3 UTIs in 12 months) and eligibility criteria compared to women who had only 1 or 2 UTIs in 12 months based on all criteria (Table 1). Specifically, women with 3 UTIs tended to be older, have a slightly higher Charlson score, and higher rates of pelvic organ prolapse, urinary incontinence, and antimicrobial prophylaxis (all p values <0.001).

Overall, 2.8% and 6.9% of women with uncomplicated recurrent UTIs underwent cystoscopy and imaging (related to a UTI diagnosis), respectively (Table 2). Thirty nine percent of women had 0 urine cultures (out of 3 UTIs) and an additional 27.7% and 20.8% had only 1 or 2 urine cultures (out of 3 UTIs), respectively. Only 12.4% of women had 3 urine cultures (out of 3 UTIs).

Table 3 presents results from propensity score models predicting downstream resource utilization among women who did and did not have urine cultures the majority (>50% or 2/3rds) of the time during the definitional period. These results indicate that having a urine culture for at least 2/3 UTIs was associated with fewer UTI related hospitalizations (OR 0.79; 95% CI 0.67, 0.93) and lower IV antibiotic use (OR 0.91, 95% CI 0.86, 0.97), while also being associated with more office visits (OR 1.06, 95% CI 1.03, 1.10) and diagnoses of pyelonephritis (OR 1.14, 95% CI 1.02, 1.27).

Comment

This study represents the first national epidemiologic study of uncomplicated recurrent UTIs in women, demonstrating an incidence of 102 per 100,000 women ages 18–64 in the United States. Incidence was demonstrated to have a bimodal age distribution and almost half (40%) of women did not have any urine culture directed care (indicated by 0 urine cultures out of 3 uncomplicated recurrent UTIs). Urine culture directed care was associated with a decrease in high cost resource utilization, as demonstrated by fewer UTI related hospitalizations and lower use of IV antibiotics.

Existing data on uncomplicated recurrent UTIs in women are limited to older studies with small sample sizes. One study published in 1990 looked at a cohort of 113 women in college and found a high rate of UTI recurrence of 27% within 6 months of an incident UTI, with 2.7% of women experiencing a second recurrence during this time period.[12] Another study published in 1996 prospectively followed 179 women ages 17 to 82 with a UTI and detected

a second UTI in 44% women over a follow-up period of 1 year.[13] More recent epidemiologic studies in women with uncomplicated recurrent UTIs are lacking.

Currently, no U.S. guidelines for uncomplicated recurrent UTIs exist. However, European and Canadian guidelines do exist for the diagnosis and treatment of uncomplicated recurrent UTIs in women. These guidelines agree that UTIs need to be diagnosed by urine culture and that imaging and cystoscopy are not routinely necessary or recommended for evaluation of this population.[6,7] While it is not our intention to hold our cohort of women with *incident* uncomplicated UTIs to these guidelines (established for women with *prevalent* uncomplicated UTIs), we felt that it would be informative to see what type of care these women received. In our study population, only 60% of women had at least one urine culture (out of 3 UTIs). While this may seem like a low number, it is consistent with published rates from a retrospective cohort study[14] and it is important to remember that this information was collected during our definitional period of uncomplicated recurrent UTIs, furthermore, these women had not yet been formally classified as having a *recurrent* natural history. Rates of additional testing (e.g., cystoscopy and imaging) were low during this time period, demonstrating agreement with and compliance to established recommendations.

Next, we wanted to investigate whether urine culture directed was associated with lower rates of downstream complications and resource utilization. What we found was an associated decrease in utilization of higher cost resources (UTI associated hospitalizations and IV antibiotic use) and an associated increase in utilization of lower cost resources and complications (UTI related office visits and pyelonephritis). The lower rate of hospitalizations and UTI associated IV antibiotic use suggests that that these patients were treated using culture directed care. Our finding that women with incident uncomplicated recurrent UTIs who had more urine cultures were associated with more UTI associated office visits may be attributable to a higher intensity of care/treatment for this condition. The finding that women with culture directed care were associated with slightly higher rates of pyelonephritis may indicate an element of endogeneity in our data, suggesting that the presence of pyelonephritis may reflect a higher severity of UTI, making it more likely that these patients would be treated with culture-driven care. Alternatively, this finding could indicate a coding error, since we would expect to see higher rates of hospitalization if more patients were having significant episodes of pyelonephritis.

These data should be interpreted with certain limitations in mind. First, this study is somewhat limited by the use of claims data to define uncomplicated recurrent UTIs. Using claims data, we were only able to capture UTIs associated with coded E&M visits, and we recognize that this represents a conservative estimate of these diagnoses. Therefore, our data underestimate the true incidence of uncomplicated recurrent UTIs in women. Additionally, by using claims data, we were unable to capture information on women with uncomplicated recurrent UTIs who do not have insurance and who were not able to seek care and be represented in these data. However, these data are instructive based on a large nationally representative sample and add important information to the literature regarding the scope and treatment implications related to this problem. These data greatly build upon former case studies and represent a valuable contribution to the literature. Second, since our sample was limited to women under the age of 65, we do not include/capture the older population of

women, who may demonstrate different incidence and different diagnostic and treatment implications. Finally, we evaluated downstream resource utilization based on a cohort of women defined as having *incident* uncomplicated recurrent UTIs. Furthermore, we acknowledge that these women had not yet met the definitional criteria of uncomplicated recurrent UTIs (3 UTIs in a 12 month period) and may differ from women with *prevalent* uncomplicated recurrent UTIs. Our objective, however, was to determine what resources were being utilized in this population and to evaluate whether women who had culture directed care were associated with different outcomes compared to those who had not. We plan to evaluate women with *prevalent* uncomplicated recurrent UTIs in future studies.

Conclusions

Overall, the incidence of incident uncomplicated recurrent UTIs in community-dwelling women ages 18–64 is 102 cases per 100,000 women. However, this likely represents a conservative estimate and the actual value may be much higher. A reasonably low number of women with this condition underwent cystoscopy and imaging for this problem, and up to 40% were treated for 3 UTIs without the use of any urine cultures. The use of urine cultures was associated with decreasing utilization of high cost resources, indicated by lower rates of UTI related hospitalizations and IV antibiotic use. These findings are helpful in guiding future guideline protocols and development for women with uncomplicated recurrent UTIs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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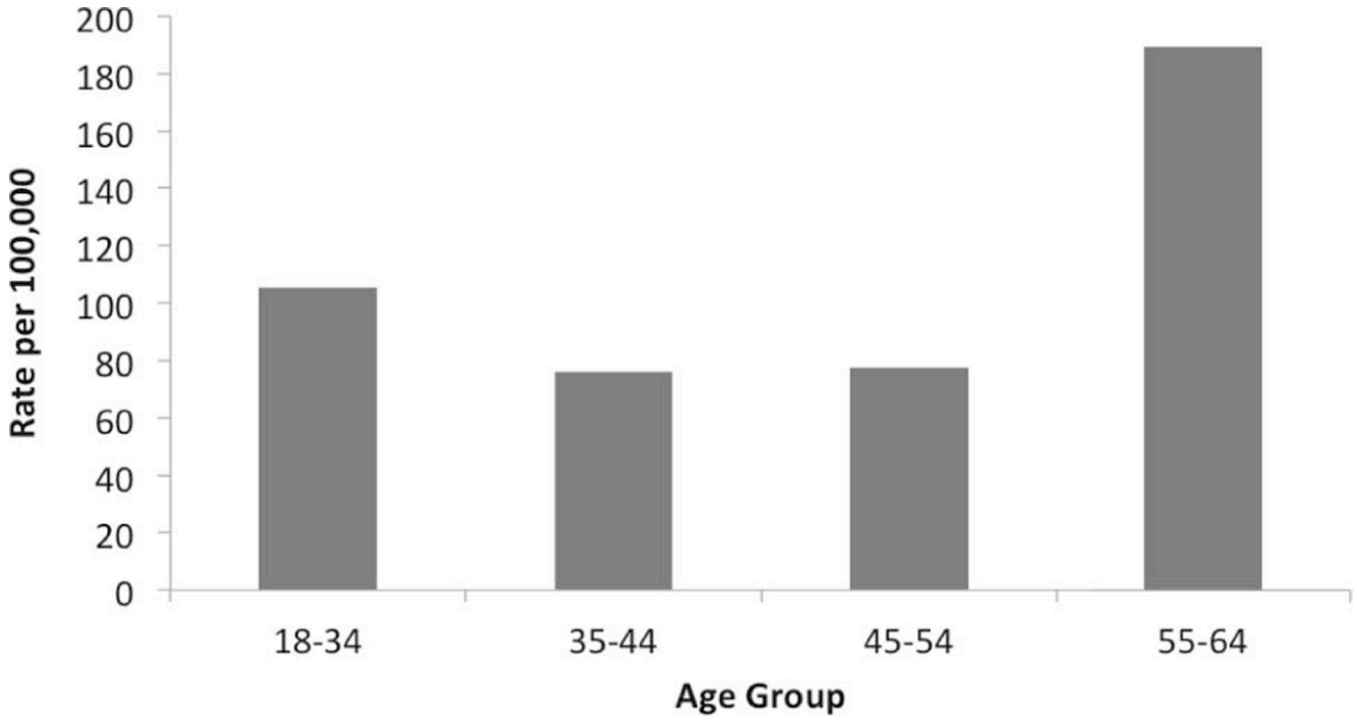

Figure 1.
Incidence of uncomplicated recurrent UTIs by age group.

Table 1

Baseline characteristics of women with 1, 2 or 3 incident uncomplicated UTIs (measured during the definitional period). P value represents difference between the 3 groups.

Characteristic	1 UTI; Number (%) N=781,090	2 UTIs; Number (%) N=129,034	3 UTIs; Number (%) N= 28,545	P value
Age				
18–24	106,348 (13.6)	14,966 (11.6)	3,269 (11.5)	<0.001
25–34	146,962 (18.8)	19,974 (15.5)	3,982 (14.0)	
35–44	181,432 (18.8)	28,729 (22.3)	5,820 (20.4)	
45–54	196,062 (25.1)	33.729 (26.2)	7,298 (25.6)	
55–64	150,286 (19.2)	31,579 (24.5)	8,176 (28.6)	
Region				
New England	28,389 (3.6)	4,347(3.4)	932 (3.3)	<0.001
Middle Atlantic	48,676 (6.2)	7,058 (5.5)	1,340 (4.7)	
East North Central	149,811 (19.2)	25,710 (19.9)	5,722 (20.1)	
West North Central	51,768 (6.6)	8,052 (6.2)	1,775 (6.2)	
South Atlantic	163,708 (21.0)	27,536 (21.3)	6,026 (21.1)	
East South Central	75,439 (9.7)	14,240 (11.0)	3,325 (11.7)	
West South Central	116,044 (14.9)	18,167 (14.1)	4,012 (14.1)	
Mountain	38,741 (4.9)	5,850 (4.5)	1,338 (4.7)	
Pacific	108,514 (13.9)	18,074 (14.0)	4,075 (14.3)	
Insurance				
Preferred Provider Organization (PPO)	463,717 (59.4)	75,055 (58.2)	16,797 (58.8)	<0.001
Comprehensive Insurance	38,309 (4.9)	7,947 (6.2)	1,967 (6.9)	
Exclusive provider organization and health maintenance organization	159,775 (20.5)	25,954 (20.1)	5,418 (19.0)	
Point-of-service Insurance	90,893 (11.6)	16,465 (12.8)	3,615 (12.7)	
Deductible health plan Insurance	28,396 (3.6)	3,613 (2.8)	748 (2.6)	

Characteristic	**1 UTI; Number (%) N=781,090**	**2 UTIs; Number (%) N=129,034**	**3 UTIs; Number (%) N= 28,545**	**P value**
Charlson Comorbidity Index				
0	748,444 (95.8)	123,158 (95.5)	26,868 (94.1)	<0.001
1	29,296 (3.8)	5,243 (4.1)	1,462 (5.1)	
2 +	3,350 (0.4)	633 (0.5)	215 (0.8)	
Pelvic organ prolapse	12,803 (1.6)	3,800 (2.9)	1,230(4.3)	<0.001
Urinary Incontinence	18,531 (2.4)	5,822 (4.5)	1,861 (6.5)	<0.001
Antimicrobial prophylaxis	2,881 (0.4)	762 (0.6)	381 (1.3)	<0.001

Table 2

UTI related diagnostic testing among women with uncomplicated recurrent UTIs.

Resource	**N (%)**
Cystoscopy	794 (2.8)
Imaging, overall	1402 (6.9)
X-Ray	341 (1.2)
CT scan	667 (2.3)
MRI	1 (0)
Urologic	514 (1.8)
Number of urine cultures (out of 3 UTIs)	
0	11162 (39.1)
1	7900 (27.7)
2	5936 (20.8)
3	3547 (12.4)

Table 3

Logistic regression to predict downstream resource utilization using propensity score matching based on having a urine culture >50% of the time during the definitional period.

	ER visit	Hospitalization	Office visit	IV antibiotics	Pyelonephritis
Urine culture >50% of the time	0.97 (0.90, 1.05)	0.79 (0.67, 0.93)	1.06 (1.03, 1.10)	0.91 (0.86, 0.97)	1.14 (1.02, 1.27)
Age 18–24	1.00	1.00	1.00	1.00	1.00
Age 25–34	0.70 (0.61, 0.79)	1.17 (0.78, 1.77)	0.97 (0.91, 1.04)	1.27 (1.12, 1.44)	0.76 (0.64, 0.92)
Age 35–44	0.51 (0.45, 0.57)	1.05 (0.71, 1.56)	1.05 (0.98, 1.12)	1.17 (1.04, 1.32)	0.58 (0.48, 0.69)
Age 45–54	0.43 (0.38, 0.49)	1.49 (1.04, 2.14)	1.07 (1.00, 1.13)	1.20 (1.07, 1.35)	0.41 (0.35, 0.49)
Age 55–64	0.40 (0.36, 0.45)	1.90 (1.34, 2.71)	1.25 (1.18, 1.33)	1.16 (1.03, 1.30)	0.35 (0.30, 0.43)
West North Central	1.00	1.00	1.00	1.00	1.00
New England	1.13 (0.89, 1.43)	0.36 (0.19, 0.67)	1.09 (0.97, 1.22)	0.25 (0.17, 0.36)	0.96 (0.65, 1.43)
Middle Atlantic	1.05 (0.85, 1.31)	0.39 (0.23, 0.66)	1.01 (0.92, 1.12)	0.52 (0.41, 0.66)	0.50 (0.32, 0.76)
East North Central	1.02 (0.86, 1.20)	0.64 (0.47, 0.88)	1.11 (1.02, 1.20)	0.83 (0.71, 0.96)	0.93 (0.71, 1.21)
South Atlantic	0.83 (0.71, 0.98)	0.63 (0.46, 0.85)	1.07 (0.99, 1.15)	0.94 (0.81, 1.09)	1.33 (1.03, 1.71)
East South Central	0.77 (0.64, 0.93)	0.47 (0.32, 0.69)	1.23 (1.13, 1.34)	3.43 (2.97, 3.96)	0.99 (0.74, 1.33)
West South Central	0.88 (0.74, 1.05)	0.78 (0.56, 1.07)	1.22 (1.13, 1.33)	2.57 (2.23, 2.96)	1.27 (0.98, 1.66)
Mountain	1.67 (1.37, 2.03)	0.29 (0.16, 0.51)	1.00 (0.90, 1.11)	1.18 (0.98, 1.42)	1.26 (0.97, 1.65)
Pacific	0.93 (0.79, 1.11)	0.45 (0.31, 0.64)	1.16 (1.07, 1.26)	0.76 (0.65, 0.89)	1.26 (0.97, 1.65)
Preferred Provider Organization (PPO)	1.00	1.00	1.00	1.00	1.00
Comprehensive Ins	0.85 (0.72, 1.01)	0.54 (0.35, 0.81)	1.01 (0.94, 1.09)	0.74 (0.64, 0.85)	1.09 (0.86, 1.38)
Exclusive provider organization and health maintenance organization	1.30 (1.18, 1.43)	1.37 (1.11, 1.69)	0.94 (0.85, 1.05)	0.79 (0.73, 0.86)	0.99 (0.86, 1.14)
Point-of-service Ins	1.04 (0.92, 1.18)	1.01 (0.76, 1.33)	0.88 (0.84, 0.93)	0.79 (0.72, 0.87)	0.91 (0.76, 1.10)
Deductible health plan Ins	1.43 (1.17. 1.75)	1.50 (0.95, 2.35)	0.95 (0.85, 1.05)	1.17 (0.98, 1.39)	0.92 (0.65, 1.31)
Charlson score 0	1.00	1.00	1.00	1.00	1.00
Charlson score 1	1.59 (1.37, 1.85)	2.65 (2.06, 3.40)	1.27 (1.17, 1.38)	1.52 (1.35, 1.71)	1.54 (1.23, 1.92)
Charlson score 2+	2.27 (1.63, 3.16)	13.50 (9.84, 18.53)	1.25 (1.01, 1.53)	2.62 (2.03, 3.39)	6.47 (4.69, 8.92)
Urinary incontinence	1.18 (1.01, 1.38)	1.96 (1.53, 2.50)	1.60 (1.48, 1.74)	1.43 (1.28, 1.59)	1.25 (1.01, 1.56)
Pelvic organ prolapse	1.15 (1.94, 1.39)	1.53 (1.12, 2.07)	1.35 (1.22, 1.48)	1.43 (1.26, 1.63)	1.44 (1.11, 1.87)

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	ER visit	Hospitalization	Office visit	IV antibiotics	Pyelonephritis
Antibiotic prophylaxis	0.60 (0.40, 0.91)	2.17 (1.39, 3.39)	1.78 (1.50, 2.11)	0.75 (0.57, 0.99)	0.96 (0.59, 1.57)