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Rates of hospitalization for urinary tract infections among medicaid-insured individuals by spina bifida status, Tennessee 2005–2013

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Abstract

Background: Individuals with spina bifida are at increased risk for urinary tract infection (UTI), however there are few population-based investigations of the burden of UTI hospitalizations.

Objective: We assessed rates and risk factors for UTI hospitalization in individuals with and without spina bifida.

Methods: We conducted a retrospective cohort study to estimate rates of UTI hospitalization by spina bifida status. We included individuals enrolled in Tennessee Medicaid who lived in one of the Emerging Infections Program's Active Bacterial Surveillance counties between 2005 and 2013. Spina bifida was primarily defined and UTI hospitalizations were identified using International Classification of Diseases, Ninth Revision diagnoses. We also studied a subset without specific health conditions potentially associated with UTI. We used Poisson regression to calculate rate ratios (RR) of UTIs for individuals with versus without spina bifida, adjusting for race, sex and age group.

Results: Over the 9-years, 1,239,362 individuals were included and 2,493 met criteria for spina bifida. Individuals with spina bifida had over a four-fold increased rate of UTI hospitalization than

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Declaration of competing interest

None declared.

those without spina bifida-in the overall study population and in the subset without specific, high-risk conditions (adjusted rate ratios: 4.41, 95% confidence intervals: 3.03, 6.43) and (4.87, 95% CI: 2.99, 7.92), respectively. We detected differences in rates of UTI hospitalization by race and sex in individuals without spina bifida that were not seen among individuals with spina bifida.

Conclusions: Individuals with spina bifida had increased rates of UTI hospitalizations, and associated demographic patterns differed from those without spina bifida.

Keywords

Hospitalization; Medicaid; Spina bifida; Urinary tract infection

Introduction

Spina bifida includes a group of congenital anomalies that result from failure of the neural tube to close during early embryogenesis, specifically involving the spinal cord and vertebral arches, with an estimated birth prevalence of 3.40/10,000 live births.[1,2] Spina bifida affects several physiological systems and morbidities include hydrocephalus, which may require ventricular shunt, paralysis that may involve the lower extremities, incontinence of bowel and bladder, and associated urinary tract infections (UTI).[2–5] Although adults and children with spina bifida have an increased risk of UTI hospitalization, the burden needs to be further delineated in a population-based sample to identify high-risk groups and inform prevention efforts.[4,6]

Although some studies have investigated UTIs in specific participant groups and clinical settings, such as febrile infants or individuals with symptoms potentially localized to the urinary tract presenting in the outpatient or inpatient setting, few have investigated rates of UTI hospitalizations in individuals with spina bifida.[4,7,8] In addition, although differences in UTIs have been reported by demographic factors such as age and race, few were conducted at the population level and it is not known whether these demographic differences are seen in individuals with spina bifida.[9] To address these gaps, we assessed rates and risk factors associated with UTI hospitalization in individuals with and without spina bifida in a multi-year retrospective cohort of individuals enrolled in Tennessee Medicaid 2005–2013.[10,11]

Methods

In a cohort of 1,239,362 individuals enrolled in the Tennessee Medicaid Program, 2005–2013, we assessed trends and differences in rates of UTI hospitalization according to spina bifida status (with and without) by demographic factors and over time. Using previously described methods, we obtained data from Tennessee Medicaid administrative data files linked with vital records.[12–14] The protocol was approved by the Institutional Review Boards of Vanderbilt University and the Tennessee Department of Health and by representatives of Tennessee Medicaid Program.

Study population and data sources

Eligible participants lived in a Tennessee (TN) county participating in the Centers for Disease Control and Prevention, Emerging Infections Program, Active Bacterial Core (ABC)

surveillance program and were continuously enrolled in Tennessee Medicaid during year of UTI hospitalization.[11,15] The Active Bacterial Core Surveillance Program is a population-based surveillance system for specific invasive bacterial pathogens that includes individuals residing in 20 major urban and surrounding rural counties during the study period, representing about 60% of the state's population.[16] All county residents who met study criteria for this current study were eligible for inclusion. For each year, 2005–2013, continuous enrollment was defined as no more than 90 days non-enrollment. Additional eligibility requirements included residing in an Active Bacterial Core surveillance county for at least one day and being younger than 65 years during a study year. Pregnant women were excluded. Demographic characteristics, chronic medical conditions, and clinical outcomes were collected from Tennessee Medicaid administrative claims databases. These databases contain enrollment files, pharmacy files, and inpatient and outpatient medical encounter data.

Primary exposure: spina bifida status

We used methods commonly employed in studies using large administrative databases to characterize our exposure and outcome. We characterized individuals with or without spina bifida through ICD-9 CM coding of healthcare encounters and vital records data. Individuals were identified as having spina bifida if they met one or more of the following criteria: 1) one or more hospitalization with a spina bifida-specific diagnosis code (741.xx, excluding cases with anencephaly, 740.00–740.10), 2) two or more outpatient visits (clinic, emergency department, and/or 23 h observation stays) separated by 7 days with a spina bifida diagnosis code, or 3) spina bifida indicated on the birth certificate.

Primary outcomes: UTI hospitalization

Individuals with UTI-associated hospitalizations were identified if they were hospitalized (including 23-h observation stays) and received a diagnosis of UTI in any of the discharge diagnosis fields (ICD-9 codes: 771.82, 590.00, 590.01, 590.10, 590.11, 590.2X, 590.3X, 590.80, 590.9X, 595.0X, 595.9X and 599.0X).[4]

Subpopulation of individuals without specific co-existing/chronic conditions

We assessed UTI hospitalization burden and relative rates in individuals with and without spina bifida in a subpopulation without concurrent diagnoses of specific co-existing/chronic conditions. Using ICD-9 diagnoses and pharmacy file prescription filling data in the year of the UTI, we excluded individuals with the following specific co-existing/chronic conditions from the sub analyses: heart disease, chronic lung disease, neurologic disorders/conditions, diabetes mellitus, acute/chronic renal disease, vesicoureteral reflux (VUR), chronic liver disease, cancer/immunodeficiency (including human immunodeficiency virus and major organ transplant), and sickle cell disease.[14] A typical diagnosis of specific co-existing/chronic conditions was characterized by one or more of the following: at least one hospitalization with an associated ICD-9 code, 2 or more outpatient visits, or filling of a condition-specific medication.

Statistical analysis

We calculated the average annual rates of UTI hospitalization among individuals with and without spina bifida, 2005–2013, as the proportion of individuals with at least one UTI hospitalization per 1,000 persons in the total cohort. We also calculated UTI hospitalization rates by race (black, white, and other), sex (male, female), and age group (less than 1 year, 1 to < 3 years, 3 to < 13 years, 13 to <18 years, and 18 years and older) separately. We estimated corresponding rate ratios (RR) along with their 95% Confidence Intervals (CI) using unconditional maximum likelihood estimation (Wald) with normal approximation (female vs. male, race and age groups using less than 1 year as referent).[17] To examine flexible smooth trends in plots, we used a moving linear regression smoother (loess) (locally weighted least squares).[18]

We used Poisson regression to calculate unadjusted and adjusted RRs of UTIs and 95% Cls for individuals with versus without spina bifida, adjusting for race, sex and age group. The robust Huber-White sandwich variance estimator was used to provide cluster-corrected standard errors and 95% Cls of the estimated RRs. We repeated analyses for subpopulation of individuals without specific coexisting/chronic conditions. Data management was carried out using SAS version 9.4 and analyses were performed using R version 3.3.2.[19]

Results

Rates of UTI hospitalization in all eligible

We identified 1,239,362 individuals, 2005–2013, who met study criteria. A total of 2,493 (0.20%) individuals were identified as having spina bifida. Overall, 57% of individuals were female, 41% were black, and 44% were white. The proportion of females (62%) and whites (58%) were higher in the spina bifida group compared to the group without spina bifida (57% female and 44% white). Individuals with spina bifida had a median age that was about 10 years older compared to individuals without spina bifida (Table 1).

Over the 9 study years, the average rate of at least one UTI hospitalization per 1,000 persons was 9.3 (95% CI: 9.2, 9.4) in the total study population. In stratified analyses, the rate in individuals with spina bifida was 68.7/1,000 compared to 9.1/1,000 for those without (unadjusted, RR 7.52, 95% CI: 7.0, 8.05). In analyses by year, rates remained stable (Fig. 1). We performed sex-stratified analysis by spina bifida status and examined UTI hospitalization rates. In the group with spina bifida, the UTI rate was 69.5/1,000 for females and 67.6/1,000 for males (RR female vs. male: 1.03, 95% CI: 0.89, 1.18). In individuals without spina bifida, the rate was 12.2/1,000 for females and 5.3/1000 for males (RR female vs. male: 2.32, 95% CI: 2.27, 2.37). Gender differences between individuals with and without spina bifida were consistent throughout study years (Fig. 2).

Age group analysis of UTI hospitalization rates revealed different patterns between those with and without spina bifida. Among individuals with spina bifida, the rate of UTI hospitalization was highest among infants less than 1 year of age (124.1/1,000 persons, referent group), followed by adults 18 years and older, (80/1,000, RR; 0.64, 95% CI: 0.40,1.04), children 1 to <3 years of age (69.2/1,000, RR: 0.56, 95% CI: 0.30,1.04), 3 to <13 years of age (37.9/1,000, RR: 0.30, 95% CI: 0.18,0.52) and 13 to <18 years of age with 33.3

UTIs per 1,000 (RR: 0.27, 95% CI: 0.15,0.47). In individuals without spina bifida, the rate in infants <1 year of age was 5.6/1,000 (referent), the rate was lower in children 13 to <18 years (1.4/1,000, RR: 0.25, 95% CI: 0.23,0.27), 1 to <3 years (1.3/1,000, RR: 0.23, 95% CI: 0.21,0.26), and 3 to <13 years (0.6/1,000, RR: 0.10, 95% CI: 0.09,0.11). The rate was highest among adults 18 years and older, 20.8/1,000 (RR: 3.7; 95% CI: 3.5,3.9). Age differences in the rates of UTI hospitalization among individuals with spina bifida were not as consistently different as those without spina bifida (Fig. 3).

We observed different patterns in UTI hospitalization rate by race by spina bifida status (Fig. 4). In individuals with spina bifida, racial differences in UTI hospitalizations were not statistically significant, RR: Black vs. white 0.85 (95% CI:0.72,1.01) and Other Race vs. White RR:1.05 (95%CI: 0.88,1.24). In individuals without spina bifida, the rate of UTI hospitalization among blacks was approximately 30% (RR: 0.71, 95% CIs: 0.69,0.72) lower than that of whites. For the overall study period, RRs from multivariable Poisson regression analysis indicated that the rate of UTI hospitalization in individuals with spina bifida was 4-fold as high as the rate in individuals without spina bifida (RR: 4.41 95%CI: 3.03,6.43). Results were similar when separate analysis by study year were carried out (data not shown).

Rates of UTI hospitalization in eligible individuals without specific chronic conditions

In a subpopulation of individuals without specific coexisting/chronic conditions, demographic characteristics were similar to the total study population (data not shown). In total, 108,018 individuals were excluded from these sub-group analyses, including 13.6% (340/2,493) of the individuals with spina bifida and 8.7% (107,678/1,239,262) of individuals without spina bifida. Overall UTI hospitalization rates were 26.6/1,000 and 3.0/1,000 for individuals with and without spina bifida, respectively, during 2005–2013. In similar aggregated rates of UTI hospitalization, females with spina bifida had a rate of 30.8/1,000 and males 20.2/1,000; whereas the rate was 4.7/1,000 for females vs. 1.0/1,000 for males without spina bifida. UTI hospitalization rates among individuals with spina bifida were lowest among children 3 to <13 and 13 to < 18 years (19.2/1,000 and 13.73/1,000) as previously noted. Infants (<1 year) had the highest rate, 50.5/1,000, however numbers were small (5/99). In participants without spina bifida the highest rates were among adults 18 years and older (7/1,000) followed by infants (4.2/1,000).

The UTI hospitalization rate was higher among Whites vs. Blacks; absolute differences were of ~2.6 per 1,000 in magnitude in those without spina bifida and ~1.9/1,000 difference in those with spina bifida. In addition, those of other race with spina bifida had a rate of UTI hospitalization that was 1.46 times as high as that for whites (RR = 1.46, 95% CI: 1.09,1.96). Overall, the adjusted rate of UTI hospitalization in individuals with spina bifida was approximately 5-fold as high as the rate among those without spina bifida (RR: 4.87 95% CI: 2.99, 7.92).

Discussion

In this retrospective cohort study we found that individuals with spina bifida experienced a higher rate of UTI hospitalization than individuals without spina bifida, with an overall rate of 68.7/1,000 compared to 9.1/1,000, respectively. For the study period, the adjusted RR of

UTI hospitalization was 4-fold higher in individuals with spina bifida than those without spina bifida (RR: 4.41 95%CI: 3.03,6.43). In the subpopulation of individuals without specific chronic health conditions, crude UTI hospitalization rates were about 2.5–3-fold lower than the overall study population. The UTI hospitalization rate was 26.6/1,000 in individuals with spina bifida compared to 3.0/1,000 in those without, with an adjusted relative rate similar to that in the overall study population.

In our previous study of UTI hospitalization rates in individuals with and without spina bifida enrolled in an employer-based insurance program, we found rates of 22.8/1,000 and 0.44/1,000, respectively.[4] Thus in our current study of individuals with spina bifida enrolled in Tennessee Medicaid compared to our previous work, rates in the lower risk population were similar to those enrolled in an employer based insurance program. We found that UTI hospitalization rates in the spina bifida and non-spina bifida populations decreased when specific preexisting/comorbid conditions were excluded. This is consistent with a number of previous findings of significant morbidity in children presenting with UTI.[9,20] When comparing rates with previous work by Armour et al., it is possible that individuals in Tennessee Medicaid may have a higher prevalence of chronic medical conditions than individuals with employer-based insurance.[4]

We examined demographic factors influencing UTI hospitalizations. When studying the relationship of age and UTI hospitalizations, the two age groups with the highest rates of UTI hospitalization were similar regardless of SB status, with spina bifida patients experiencing the highest rate of UTI hospitalization in infancy, followed by adults 18 years and older. Patients without spina bifida had the highest relative risk in the 18 years and older age group, followed by infants. The trends were similar in the lower risk subpopulation.

Interestingly, we found differences in rates of UTI hospitalization by race in the general population without spina bifida that were not detected in the group with spina bifida. In the overall population without spina bifida, whites had a rate approximately 1/3 higher than the rates for blacks and individuals of other race. Although there is limited data in the literature regarding associations of race and UTI hospitalization, a study of UTIs in febrile children less than 2 years presenting to the emergency department found that the UTI rate in black children was lower than that of white children.[7] Circumcision in male infants is also associated with decreased risk of UTI in the first year of life,[21] however in our study, only about 4% percent of the individuals without spina bifida (2005–2013) studied represent the infant population thus racial differences in circumcision rates would unlikely influence study findings. Differences in UTI hospitalization rates by race were also detected in analyses of the subpopulation that excluded individuals with VUR, therefore racial differences in VUR would not be expected to account for findings.[22] Reasons for our findings are not known, but potentially may be related to differences in factors such as underlying physiology, health behaviors, access to care, or health care quality, and future work in large population-based cohorts will be informative. We did not detect racial differences in UTI hospitalization rates in individuals with spina bifida, suggesting that spina-bifida associated complications diminish differences that may be associated with other demographic factors.

Sex was a risk factor associated with UTI hospitalization, primarily in the population without spina bifida. In the population without spina bifida, females had a more than 2-fold increased relative risk of UTI hospitalization compared to males. However, UTI hospitalization rates were similar between males and females with spina bifida. These findings reinforce that sex is an important factor to consider when considering UTI risk in the general study population; however, it could play a lesser role in UTI risk in in dividuals with spina bifida.

Our study has limitations. Although the counties covered in the TN Active Bacterial Core Surveillance Program represents approximately 60% of the State's population, findings may not be applicable to individuals with spina bifida in TN who are not living in or near urban areas.

We used ICD-9 codes to identify spina bifida status, UTI hospitalizations, and chronic conditions, which may have led to some misclassification including identifying individuals with asymptomatic bacteriuria as having UTI. In particular, individuals with spina bifida are at higher risk of developing asymptomatic bacteriuria and potentially being screened for a urinary tract infection during a hospitalization, which could lead to differential misclassification (selection bias) and a spurious increase in the association of spina bifida and UTIs. Thus, results should be interpreted with caution. Studies are needed that include chart review confirmation to provide a better understanding of the extent of the potential bias and will be helpful in informing future, large population-based studies. The associations between spina bifida and UTI hospitalization remained consistent in the studied subpopulation, although the rate of our outcome was expectedly lower. Although we characterized individuals by race, we did not characterize by ethnicity. Although we accounted for age, race and sex in estimates of the ratios of UTI hospitalization rates among those with and without spina bifida, other unmeasured factors might have influenced results. Our study included individuals enrolled in Medicaid, a population that is likely enriched with individuals with spina bifida and other chronic conditions, therefore results may not be generalizable to the non-Medicaid population.

Conclusion

The rate of UTI hospitalization in individuals with spina bifida was four-fold the rate among individuals without spina bifida. This difference in UTI hospitalization rates remained consistent over the study period in the overall study population and in the subset without specific chronic medical conditions. UTI hospitalization rate differences by race and sex that were found in the general population were not detected among individuals with spina bifida. However, UTI hospitalizations occurred most often during infancy and adulthood for those with and without spina bifida. These data suggest that certain groups are at higher risk for UTIs and reinforce the importance of efforts to decrease the UTI rate in individuals with spina bifida.

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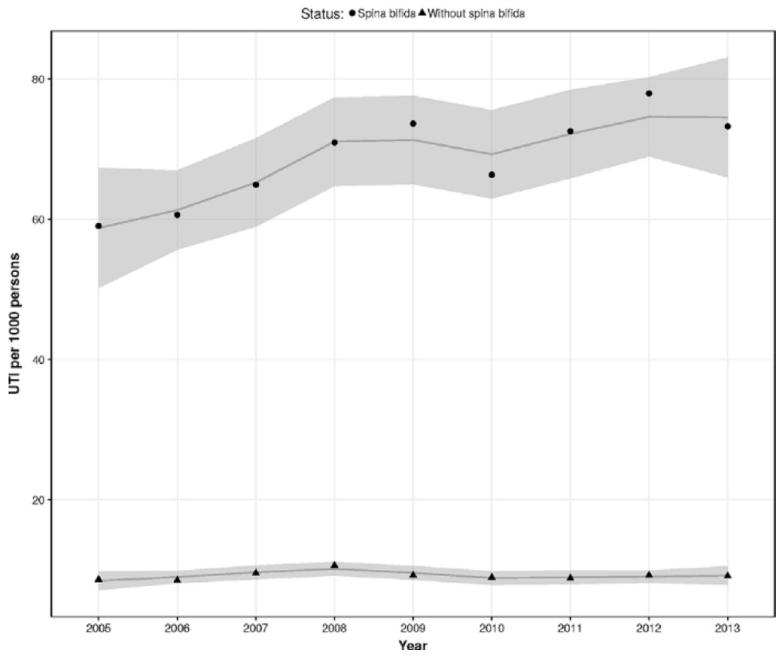

Fig. 1.

Rates of urinary tract infection hospitalization by spina bifida status, Tennessee Medicaid Enrollees, 2005–2013. Points and trend lines are shown for spina bifida and non-spina bifida groups. Trend lines were sketched using a locally weighted scatterplot smoothing curve (LOWESS).

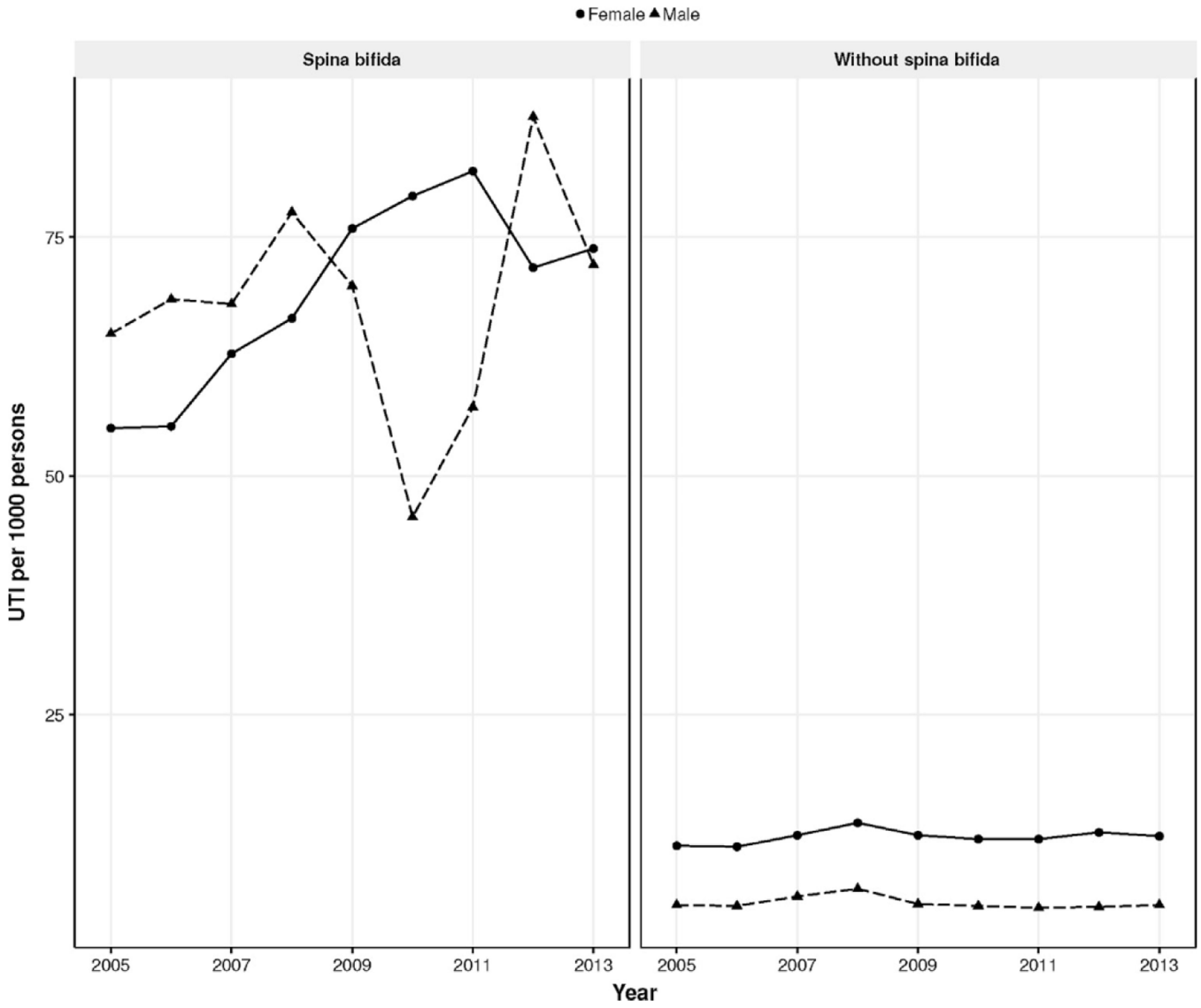

Fig. 2.

Rates of urinary tract infection hospitalization by spina bifida status and sex, Tennessee Medicaid Enrollees, 2005–2013.

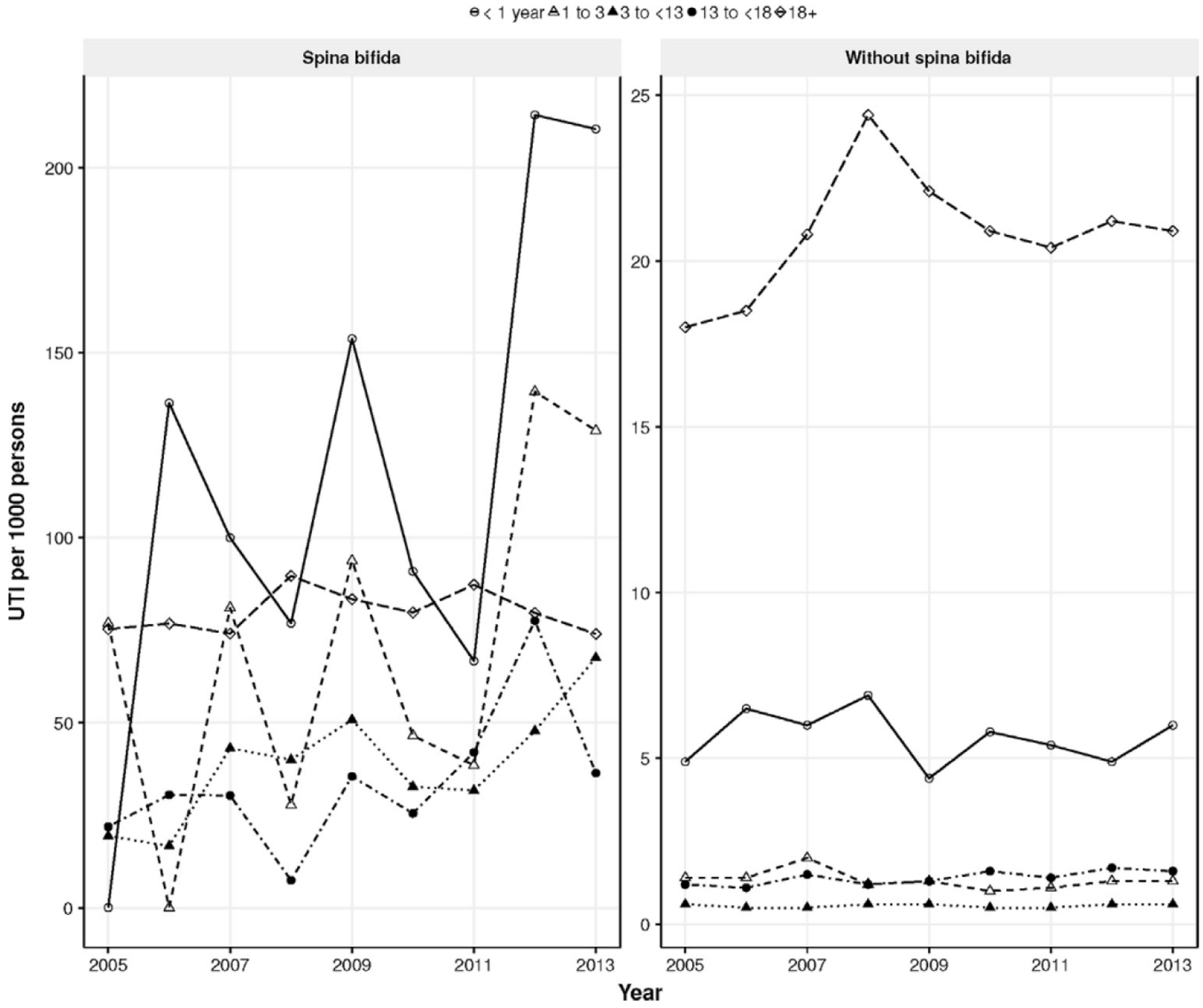

Fig. 3.

Rates of urinary tract infection hospitalization by spina bifida status and age groups, Tennessee Medicaid Enrollees, 2005–2013. Separate axes are used for spina bifida and non-spina bifida for visual ease of discerning rates in groups with low rates that were similar.

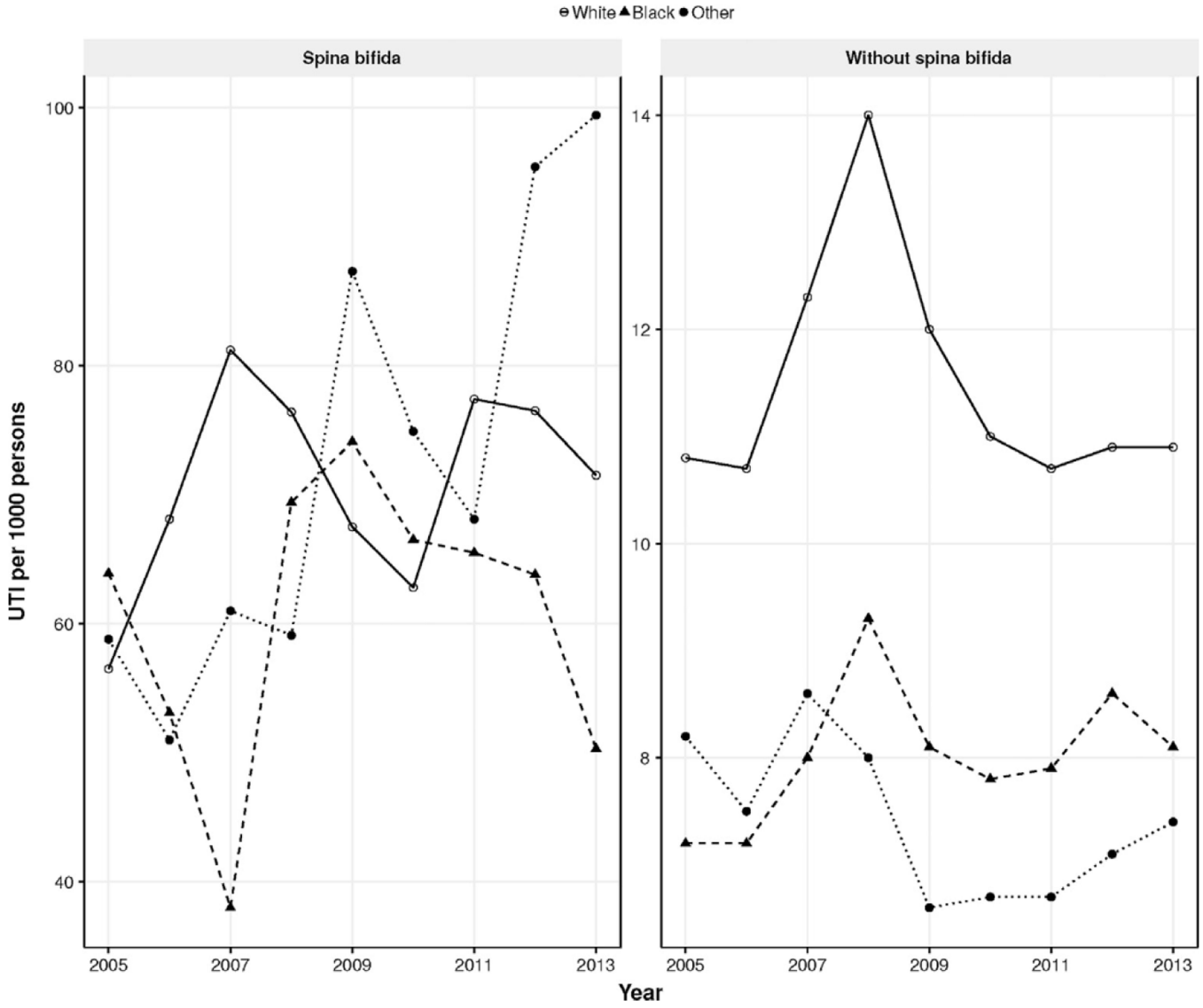

Fig. 4.

Rates of urinary tract infection hospitalization by spina bifida status and race, Tennessee Medicaid Enrollees, 2005–2013.

Table 1

Characteristics of Tennessee medicaid enrollees with and without spina bifida, 2005–2013 (n = 1,239,362).

Characteristic	%	Without Spina Bifida (n = 1,236,869)	%	With Spina Bifida (n = 2,493)
Race				
African American	41		22	
Caucasian	44		58	
Other	15		20	
Sex				
Female	57		62	
Male	43		38	
Age, years		Median [1QR]		Median [1QR]
2005		16.0[7.0,32.0]		25.0[14.0,38.0]
2006		16.0[7.0,32.0]		26.0[15.0,39.0]
2007		17.0[7.0,32.0]		26.0[15.0,39.0]
2008		17.0[7.0,32.0]		27.0[16.0,40.0]
2009		17.0[7.0,32.0]		28.0[16.0,41.0]
2010		17.0[7.0,32.0]		28.0[17.0,41.0]
2011		18.0[8.0,33.0]		29.0[17.0,42.0]
2012		18.0[8.0,33.0]		30.0[18.0,43.0]
2013		19.0[8.0,33.0]		30.0[19.0,43.0]

Abbreviations: IQR: Interquartile range, 25th and 75th percentile.