

# Rurality of Residence and Inappropriate Antibiotic Use for Acute Respiratory Infections Among Young Tennessee Children

Keerti L. Dantuluri,<sup>1,⊕</sup> Jean Bruce,<sup>2</sup> Kathryn M. Edwards,<sup>1</sup> Ritu Banerjee,<sup>1</sup> Hannah Griffith,<sup>2,⊕</sup> Leigh M. Howard,<sup>1,a</sup> and Carlos G. Grijalva<sup>2,a,⊕</sup>

<sup>1</sup>Department of Pediatrics (Infectious Diseases), Vanderbilt University Medical Center, Nashville, Tennessee, USA <sup>2</sup>Department of Health Policy, Vanderbilt University Medical Center, Nashville, Tennessee, USA

**Background.** Antibiotic use is common for acute respiratory infections (ARIs) in children, but much of this use is inappropriate. Few studies have examined whether rurality of residence is associated with inappropriate antibiotic use. We examined whether rates of ARI-related inappropriate antibiotic use among children vary by rurality of residence.

**Methods.** We conducted a retrospective cohort study of children aged 2 months–5 years enrolled in Tennessee Medicaid between 2007 and 2017 and diagnosed with ARI in the outpatient setting. Study outcomes included ARI, ARI-related antibiotic use, and ARI-related inappropriate antibiotic use. Multivariable Poisson regression was used to measure associations between rurality of residence, defined by the US Census Bureau, and the rate of study outcomes, while accounting for other factors including demographics and underlying comorbidities.

**Results.** A total of 805 332 children met selection criteria and contributed 1 840 048 person-years (p-y) of observation. Children residing in completely rural, mostly rural, and mostly urban counties contributed 70 369 (4%) p-y, 479 121 (26%) p-y, and 1 290 558 p-y (70%), respectively. Compared with children in mostly urban counties (238 per 1000 p-y), children in mostly rural (450 per 1000 p-y) and completely rural counties (468 per 1000 p-y) had higher rates of inappropriate antibiotic use (adjusted incidence rate ratio [aIRR] = 1.34, 95% confidence interval [CI] = 1.33–1.35 and aIRR = 1.33, 95% CI = 1.32–1.35, respectively).

**Conclusions.** Inappropriate antibiotic use is common among young children with ARI, with higher rates in rural compared with urban counties. These differences should inform targeted outpatient antibiotic stewardship efforts.

**Keywords.** inappropriate antibiotics; pediatrics; rural health.

Antibiotics are the most commonly prescribed medications for young children, with outpatient acute respiratory infections (ARIs), such as otitis media and pharyngitis, being the most frequently diagnosed conditions associated with their use [1, 2]. Although antibiotics are often necessary, they are commonly used inappropriately [3]. The Centers for Disease Control and Prevention defines inappropriate antibiotic use as “prescribing antibiotics when not in accordance with national and local evidence-based guidelines, wrong selection of antibiotics, wrong dosing of antibiotics, or wrong duration of antibiotics” [4]. Strategies to reduce inappropriate antibiotic use are needed to

decrease development and transmission of antibiotic-resistant organisms, reduce healthcare costs, and prevent adverse drug events [5, 6].

Although inappropriate antibiotic prescribing is common among children, the reasons for this are not well understood [3, 7–9]. Rates of inappropriate outpatient antibiotic prescribing practices vary based on provider experience, specialty, and clinical setting [10]. Some studies suggest that antibiotic prescribing may vary based on rurality of patient residence, with higher inappropriate prescribing in nonurban settings [11, 12].

Although pediatric antibiotic use is common in the United States, especially southern states, few studies have examined antibiotic prescribing practices within individual southern states [8]. In 2002, Perz et al [13] measured antibiotic prescription rates among Tennessee children living in 4 urban counties and found that Knox county had the highest rates of pediatric antibiotic use and prevalence of penicillin resistance among invasive pneumococcal infections. A more recent cross-sectional study reported that pediatricians in rural Tennessee counties prescribe antibiotics in a higher proportion of encounters than those in urban counties [14]. Although these studies provide helpful insight into patterns of antibiotic use within the state, they did not evaluate clinical conditions associated with

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<sup>a</sup>L. M. H. and C. G. G. contributed equally to this manuscript.

Correspondence: Keerti L. Dantuluri, MD, MPH, Division of Pediatric Infectious Diseases, Levine Children’s Hospital at Atrium Health, 1001 Blythe Blvd., Suite 200E, Charlotte, NC 28203 (keerti.dantuluri@atriumhealth.org).

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antibiotic prescribing, and thus a detailed examination of inappropriate antibiotic use in Tennessee is lacking.

Potentially inappropriate antibiotic use is particularly relevant for children enrolled in Tennessee Medicaid, who represent more than one half of all children born in the state [15, 16]. We sought to characterize the association between rurality of residence and the rates of ARI-related inappropriate antibiotic use among children enrolled in Tennessee Medicaid (TennCare) from 2007 to 2017.

## METHODS

### Study Design and Population

We conducted a retrospective cohort study of young children in Tennessee and compared rates of ARI, ARI-related antibiotic use, and ARI-related inappropriate antibiotic use among children residing in completely rural (CR), mostly rural (MR), and mostly urban (MU) counties. Our cohort included children 2 months to 5 years of age enrolled in TennCare for at least 180 days (at least 60 days for children aged 2–6 months) from July 1, 2007 through June 30, 2017. We excluded children with primary immunodeficiencies, neutropenia, pancytopenia, history of transplantation, sickle cell disease, cystic fibrosis, asplenia, bronchopulmonary dysplasia, and malignancy due to presumed increased risk of ARI and associated antibiotic use in children with these conditions. We excluded children with cystic fibrosis and bronchopulmonary dysplasia, as opposed to those with asthma or reactive airway disease, because they may have chronic changes on their radiographic imaging, making it difficult to interpret acute changes.

Our study used enrollment files and healthcare utilization data, including clinical encounters and pharmacy dispensing information, supplemented with state vital registries data, which included birth and death certificates. This study was approved by the Institutional Review Boards of Vanderbilt University Medical Center, the Tennessee Department of Health, and the Division of TennCare. Informed consent was not obtained because this was an analysis of deidentified and retrospective clinical data.

### Exposure: Rurality

Rurality was classified into 3 groups according to the US Census Bureau definition [17], based upon residential population density and land-use characteristics at the county level. County-level classification was chosen to determine in which counties outpatient stewardship programs could potentially target their efforts. Counties with 100% of the population living in rural areas were classified as CR, those with 50%–99.9% of the population living in rural areas were classified as MR, and those with <50% of the population living in rural areas were classified as MU [17]. Changes in county of residence were captured so that rurality classifications could change over time.

### Follow-Up

Follow-up started at the earliest time when children met selection criteria and continued until loss of enrollment in TennCare, death, end of study period, or meeting any exclusion criteria, whichever came first.

### Acute Respiratory Infections

We identified ARI-related emergency department and outpatient encounters using *International Classification of Diseases, 9th and 10th Revisions* (ICD-9 and ICD-10 codes) (Supplementary Table 1) [3, 18]. Encounters with codes for both ARI and nonrespiratory infections (Supplementary Table 2) were not considered ARI outcomes because antibiotic use may have been driven by a nonrespiratory coinfection [19].

### Acute Respiratory Infections-Related Antibiotic Use

We used pharmacy records, which have been shown to accurately estimate medication consumption in community patients enrolled in Medicaid [20], to calculate ARI-related antibiotic use. We identified oral antibiotics dispensed for ARI within 72 hours of an outpatient or emergency department encounter using pharmacy claims data (Supplementary Table 3). Intramuscular and intravenous antibiotics administered within 72 hours of the ARI encounter were identified using pharmacy and/or Healthcare Common Procedure Coding System codes. If multiple prescriptions were filled within 72 hours, we considered only the first antibiotic prescription, because this would represent the first intention to treat.

### Acute Respiratory Infection-Related Inappropriate Antibiotic Use

We classified ARI-related antibiotic use using a mutually exclusive, 3-tier classification system published by Fleming-Dutra et al [3] and outlined in Supplementary Table 1. Tier 1 includes ARI diagnoses for which antibiotics are almost always indicated, tier 2 includes diagnoses for which antibiotics are sometimes indicated, and tier 3 includes diagnoses for which antibiotics are almost never indicated. If an encounter was associated with multiple ARI diagnoses encompassing more than 1 tier, priority was given to the tier 1 diagnoses, followed by tier 2 and tier 3. Thus, inappropriate antibiotic use was classified as an antibiotic prescription associated with a tier 3 ARI diagnosis, in the absence of a tier 1 or tier 2 ARI diagnosis.

### Covariates

We classified each person-day of follow-up by calendar year, calendar month, gender, race, age, estimated median household income, and recent antibiotic exposure (any antibiotic dispensation in the prior 6 months). We also classified person-days by the history of the following underlying comorbidities: reactive airway disease or asthma, type 1 diabetes, and/or congenital heart disease. In addition, we classified each person-day by chronic glucocorticoid use, defined by a pharmacy fill of

prednisone, prednisolone, methylprednisolone, dexamethasone, hydrocortisone, beclomethasone, betamethasone, or triamcinolone with a duration of  $\geq 14$  days filled during the prior 14–30 days.

### Statistical Analysis

We calculated crude incidence rates of our primary outcomes that were decided a priori: ARI, ARI-related antibiotic use, and ARI-related inappropriate antibiotic use. Follow-up person-time was the denominator for all incidence rate calculations. For denominator calculations, we excluded the 20 person-days after an ARI, because additional encounters during this period were assumed to be related to the initial diagnosis [21]. We also excluded all person-days during periods of hospitalization, when children were not at risk for outpatient ARI, and 30 person-days after hospitalization, because ARI during that period could be related to the previous hospitalization. We used multivariable Poisson regression to compare incidence rates for each outcome among children who live in CR, MR, and MU counties, adjusting for study covariates. We also calculated adjusted rate differences for CR and MR counties relative to MU counties by multiplying the rate in MU counties times the corresponding adjusted incidence rate ratio minus 1. We also assessed changes in rates of outcomes over time. We performed subgroup analyses of racial and median household income groups, our secondary outcomes that were decided post hoc, by including interaction terms for race and rurality and median household income, respectively, in the regression model. In a separate analysis restricted to children who were diagnosed with ARI, we calculated the proportion of ARI events associated with appropriate and inappropriate antibiotic use. We also calculated the trend of these proportions over time. All analyses were conducted using Stata 15.1.

## RESULTS

### Characteristics of Study Cohort

A total of 812 271 children met cohort selection criteria, but 6939 (0.9%) children were excluded due to missing county, age, and/or sex data. The remaining 805 332 children contributed 1 840 048 person-years (p-y) of follow-up. Children residing in CR counties contributed 70 369 (4%) p-y, children residing in MR counties contributed 479 121 (26%) p-y, and children residing in MU counties contributed 1 290 558 p-y (70%). Almost half of all person-time was contributed by females, and 60% of person-time was contributed by children 2–5 years of age. Racial distribution varied by rurality of residence, with white children contributing 83% and 94% of person-time in MR and CR counties, respectively, but only 45% of person-time in MU counties. The majority of person-time was contributed by children with estimated median household incomes of \$30 000–\$50 000, and the majority of person-time contributed by children from this income bracket lived in MR and CR counties. Almost one half

of person-time contributed by children living in MR and CR counties was associated with a recent history of antibiotic exposure, whereas only 35% of person-time contributed by children living in MU areas was associated with prior antibiotic exposure (Table 1).

The crude rate (per 1000 p-y) of ARI was highest among children aged 2–12 months (2632), white children (2301), and during December (2655). The crude rate of ARI-related antibiotic use and inappropriate antibiotic use was highest among children aged 12–24 months (1339 and 380, respectively), white children (1233 and 367, respectively), and during December (1423 and 458, respectively).

### Association of Rurality of Residence With Rates of Acute Respiratory Infections (ARI), ARI-Related Antibiotic Use, and ARI-Related Inappropriate Antibiotic Use

Rates of ARI, ARI-related antibiotic use, and ARI-related inappropriate antibiotic use were higher in children who lived in MR or CR counties compared with those in MU counties (Table 2). These associations remained statistically significant after adjustment for study covariates in multivariable regression analyses (Table 2). In this analysis, young age (2–12 months), white race (see Supplementary Table 4 and subgroup analysis), and presentation during December were associated with higher rates of ARI, ARI-related antibiotic use, and inappropriate antibiotic use ( $P < .001$ ).

### Adjusted Rate Differences of Inappropriate Antibiotic Use by Rurality of Residence

Within our cohort, 307 023 ARI-related inappropriate antibiotics were prescribed for children residing in MU counties, 215 746 inappropriate antibiotics for children residing in MR counties, and 32 950 inappropriate antibiotics for children residing in CR counties. The adjusted rate difference of ARI-related inappropriate antibiotic use was 81 and 79 prescriptions per 1000 p-y higher in children living in MR and CR counties, respectively, than among children living in MU counties.

### Trend in Rates of Acute Respiratory Infections and Antibiotic Use

During the study period, crude rates of ARI, ARI-related antibiotic use, and ARI-related inappropriate antibiotic use decreased over time (Supplementary Figure 1A). The multivariable regression models indicated that the rate of ARI decreased by approximately 0.8% each year, the rate of ARI-related antibiotic use decreased by 1.3% each year, and the rate of ARI-related inappropriate antibiotic use decreased by 6.8% each year ( $P < .001$ ). These declines were consistently observed across MU, MR, and CR counties (Supplementary Figure 1B and C).

### Subgroup Analysis by Race

The strength of the association between rurality of residence and incidence of study outcomes varied by race (Figure 1), with higher IRR of ARI, ARI-related antibiotic use, and inappropriate

**Table 1. Characteristics of Study Population According to Rurality of Residence (July 1, 2007–June 30, 2017)**

Characteristic	Rurality of Residence		
	Mostly Urban	Mostly Rural	Completely Rural
Person-years (no.)	1 290 558	479 121	70 369
Age (%) <sup>a</sup>			
2–12 months	18.7	19.0	18.9
12–24 months	20.5	20.3	20.2
24–60 months	60.7	60.6	60.9
Male sex (%)	50.8	51.1	51.2
Race (%)			
White	45.3	83.2	94.3
Black	42.3	10.5	2.9
Hispanic	8.6	4.2	1.3
Other/unknown	3.8	2.1	1.6
Median Household Income (%)			
<\$30 000	29.1	18.8	17.7
\$30 000–\$50 000	38.6	54.1	67.4
\$50 000–\$70 000	19.5	17.7	9.2
>\$70 000	7.7	2.7	1.0
Missing	5.1	6.7	4.7
Recent antibiotic exposure (%)	34.8	47.9	49.3
Comorbidities (%)	4.7	4.8	3.9
Chronic glucocorticoid use (%)	1.2	0.8	0.7
Calendar Month (%)			
January	8.3	8.2	8.2
February	7.6	7.4	7.4
March	8.4	8.3	8.3
April	8.3	8.3	8.3
May	8.6	8.7	8.7
June	8.5	8.6	8.7
July	8.7	8.9	9.0
August	8.7	8.8	8.8
September	8.2	8.2	8.1
October	8.4	8.4	8.4
November	8.1	8.0	8.0
December	8.3	8.2	8.2
Calendar Year (%)			
2007	4.5	4.6	4.6
2008	9.1	9.3	9.3
2009	9.4	9.6	9.8
2010	9.9	10.1	10.3
2011	10.0	10.0	10.0
2012	9.8	9.7	9.6
2013	9.6	9.4	9.4
2014	10.0	9.8	9.7
2015	10.9	10.7	10.6
2016	11.4	11.4	11.2
2017	5.4	5.4	5.4

<sup>a</sup>Percentages reflect proportions of person-time contributed by each category.

antibiotic use among black children than among white or Hispanic children ( $P < .001$  for interaction terms) (Supplementary Table 5).

#### Subgroup Analysis by Median Household Income

The strength of association between rurality of residence and incidence of study outcomes also varied by median household income, with higher IRR or ARI, ARI-related antibiotic use, and inappropriate antibiotic use among children from lower median

household incomes compared with those from higher median household incomes (Supplementary Table 6).

#### Proportion of Acute Respiratory Infections Events Associated With Antibiotics

A greater proportion of ARI in MR (57%; 664 503 of 1 170 838) and CR (59%; 103 436 of 175 369) counties were associated with antibiotic use than ARI in MU counties (47%;

**Table 2. Incidence Rates and Incidence Rate Ratios of ARI, ARI-Related Antibiotic Use, and ARI-Related Inappropriate Antibiotic Use Among Children According to Rurality of Residence (2007–2017)**

Rurality of Residence	Person-Years	Number of Events	Crude Rate (per 1000 Person-Years)	Unadjusted IRR (95% CI)	<sup>a</sup> Adjusted IRR (95% CI)
<b>ARI</b>					
Mostly urban	1 290 558	2 269 200	1758	1.0 (Reference)	1.0 (Reference)
Mostly rural	479 121	1 170 838	2444	1.39 (1.39–1.39) <sup>b</sup>	1.07 (1.07–1.08) <sup>b</sup>
Completely rural	70 369	175 369	2492	1.42 (1.41–1.42)	1.07 (1.06–1.07)
<b>ARI-Related Antibiotic Use</b>					
Mostly urban	1 290 558	1 086 476	842	1.0 (Reference)	1.0 (Reference)
Mostly rural	479 121	664 503	1387	1.65 (1.64–1.65)	1.15 (1.14–1.15)
Completely rural	70 369	103 436	1470	1.75 (1.73–1.76)	1.17 (1.16–1.18)
<b>ARI-Related Inappropriate Antibiotic Use</b>					
Mostly urban	1 290 558	307 023	238	1.0 (Reference)	1.0 (Reference)
Mostly rural	479 121	215 746	450	1.89 (1.88–1.90)	1.34 (1.33–1.35)
Completely rural	70 369	32 950	468	1.97 (1.95–1.99)	1.33 (1.32–1.35)

Abbreviations: ARI, acute respiratory infection; CI, confidence interval; IRR, incidence rate ratio.

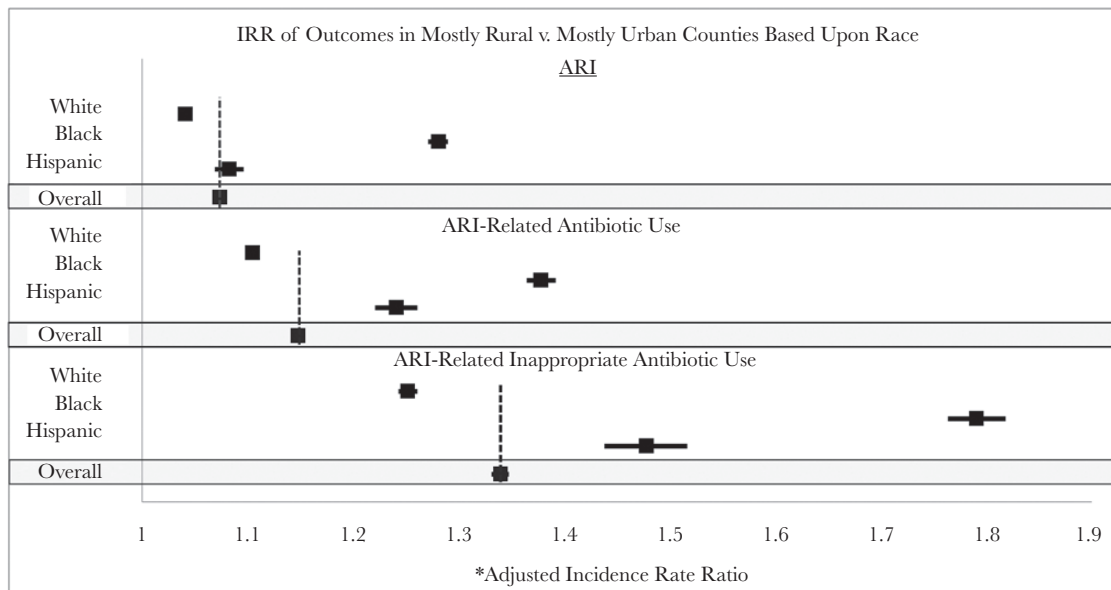
<sup>a</sup>Covariates accounted for in the multivariable regression model: calendar year/month, gender, race, age, median household income, recent antibiotic exposure, underlying comorbidities, history of chronic glucocorticoid use.

<sup>b</sup>CI appears to overlap due to rounding.

1 086 476 of 2 269 200) ( $P < .001$  for each comparison). Likewise, a greater proportion of ARI in MR (18%; 215 746 of 1 170 838) and CR (19%; 32 950 of 175 369) counties were associated with inappropriate antibiotic use than in MU counties (14%; 307 023 of 2 269 200) ( $P < .001$  for each comparison). Within MU, MR, and CU counties, the proportion of ARI associated with antibiotic use and inappropriate antibiotic use (Figure 2) declined overtime ( $P < .001$  based upon multivariable regression).

## DISCUSSION

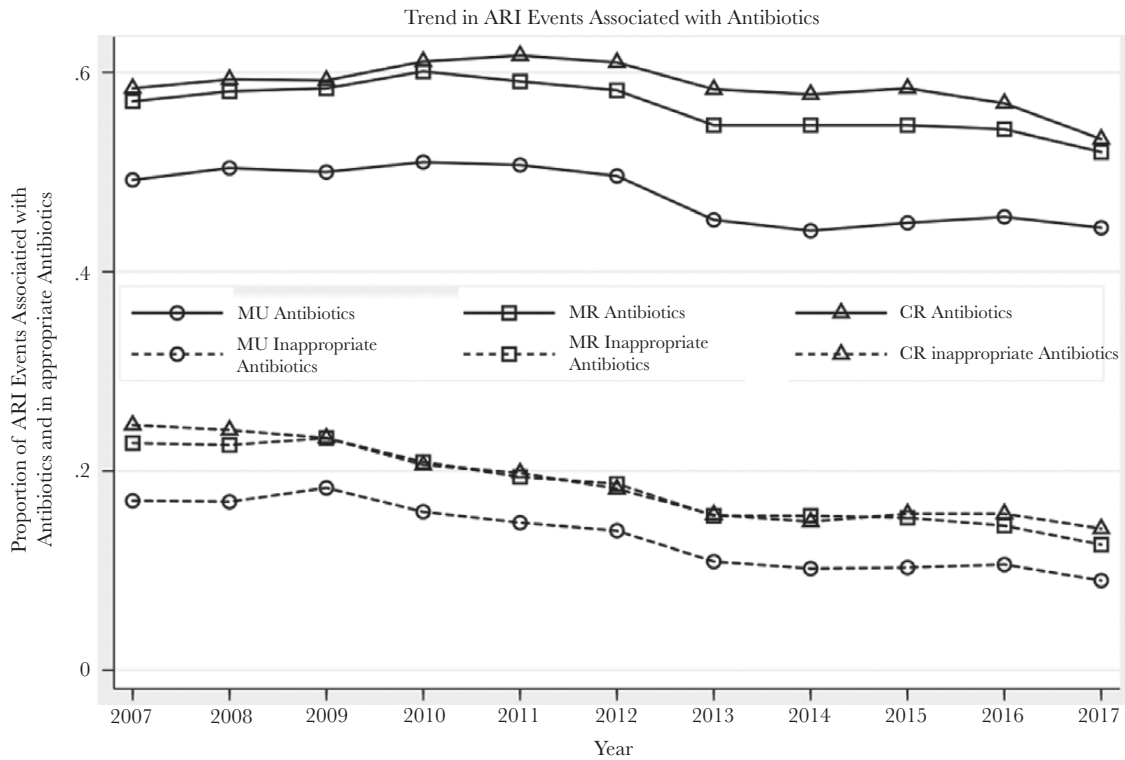
In our study, rates of ARI, ARI-related antibiotic use, and ARI-related inappropriate antibiotic use were higher among children who lived in mostly or CR counties compared with children who lived in MU counties. Although rates of these outcomes and the proportion of ARI associated with overall and inappropriate antibiotic use decreased over time, the proportion of ARI associated with overall and inappropriate antibiotic use remained higher in children living in rural counties



\*Covariates: calendar year/month, gender, race, age, median household income, recent antibiotic exposure, underlying comorbidities, history of chronic glucocorticoid use

**Figure 1.** Incidence rate ratios of acute respiratory infection (ARI), ARI-related antibiotic use, and ARI-related inappropriate antibiotic use among children of different race groups who live in mostly rural versus mostly urban counties. Vertical axis represents racial group for each outcome and horizontal axis represents incidence rate ratio and 95% confidence intervals.





**Figure 2.** Trend in the proportion of children enrolled in Tennessee Medicaid between 2007 and 2017 and diagnosed with acute respiratory infection (ARI) who received antibiotics and inappropriate antibiotics based upon rurality of county of residence. Solid lines represent overall antibiotic use, and dotted lines represent inappropriate antibiotic use. Mostly urban (MU) counties are represented by circles, mostly rural (MR) counties are represented by squares, and completely rural (CR) counties are represented by triangles.

compared with urban counties throughout the study period. The strength of association of rurality and rate of antibiotic use was higher among black children and children from lower median household incomes.

The relative rate of ARI was slightly higher in children living in rural counties compared with urban counties. Although there is no conclusive explanation for higher rates of ARI in rural areas, several factors may be postulated to play a role. In our study, individuals living in rural counties tended to live in lower income households, which may be associated with challenges to accessing healthcare, potentially leading to less preventative care, lower vaccine coverage [22], and more severe illness at presentation [23]. Children in rural settings may also be exposed to more household mold [24–26] and second hand tobacco exposure [27], which predispose children to respiratory illnesses [28, 29]. Furthermore, there were larger representations of white children in rural counties than in urban counties in our study, and prior studies have shown that white children receive more diagnoses of ARI compared with children of other races even when they are treated by the same clinician [30]. Overdiagnosis in white children and/or underdiagnosis in minority children may have played a role in the higher rates of ARI observed in rural counties.

We observed higher rates of inappropriate antibiotic use among children living in rural counties compared with urban counties, with approximately 80 more inappropriate prescriptions per 1000 p-y in rural counties compared with urban counties. Earlier studies conducted both outside and in Tennessee have reported higher antibiotic use among individuals living in nonurban counties compared with urban counties, but the appropriateness of the antibiotic use was not assessed [11, 12, 14]. Our findings complement those previous observations. An explanation for the higher rates of antibiotic use and inappropriate antibiotic use in children living in rural counties might be that fewer primary care providers, particularly pediatricians, practice in rural communities compared with urban settings [31]. Prior studies have shown that antibiotic prescribing by providers at nonpediatric facilities is higher when compared with those at pediatric facilities [32]. Pediatricians who work at pediatric facilities are also more likely to have academic affiliations and exhibit increased familiarity and compliance with pediatric-specific guidelines [32]. Our finding of a greater proportion of person-time associated with a history of recent antibiotic exposure among children living in rural counties, with less access to pediatric facilities, compared with those in urban counties supports this theory.

We also found that white children were more likely than black children to be diagnosed with ARI and receive antibiotics, an observation consistent with findings from other studies [30, 33]. These differences in rates based upon race raised the question of how much of the differences in antibiotic prescriptions based upon rurality may have been driven by racial disparities. However, our subgroup analysis revealed that even within individual racial groups, rural county of residence was still associated with higher rates of ARI and ARI-related antibiotic use and inappropriate antibiotic use, and this association was stronger among minority races, who were less represented in rural counties in our study. Our cohort also had an increased proportion of p-y contributed by children from lower median household incomes in rural counties compared with urban counties. However, even within individual income groups, our subgroup analysis revealed that rural county of residence was associated with higher rates of ARI and ARI-related antibiotic use and inappropriate antibiotic use, and the association was stronger among children from lower median household income groups. Our findings are similar to the results of a cross-sectional study measuring antibiotic use in adults enrolled in Medicare, where adults from lower household incomes were prescribed a higher rate of antibiotics [34]. Outpatient stewardship programs should take note that higher rates of inappropriate antibiotic use takes place in rural counties, and this problem seems to be magnified in rural-residing minority children and children from lower household incomes.

Our finding that rates of ARI and ARI-related appropriate and inappropriate antibiotic use decreased over time is consistent with previous reports from private health insurance plans [1, 35]. One explanation for the decline in ARI could be the introduction of 13-valent pneumococcal conjugate vaccine in 2010, which led to reductions in the incidence of respiratory infections [21, 36–38]. However, findings are mixed with regards to whether these declines are associated with reduced antibiotic prescriptions [21, 39]. In addition, updated guidelines for treatment of community-acquired pneumonia, streptococcal pharyngitis, and acute otitis media released between 2011 and 2013 [40–42] could have contributed to optimized diagnosis and reductions in antibiotic prescriptions. Furthermore, increasing national and international attention to antibiotic overuse and the need for stewardship may have stimulated both providers and parents to reduce inappropriate antimicrobial use [43].

More importantly, a greater proportion of ARI in rural counties were associated with overall and inappropriate antibiotic use compared with ARI in urban counties throughout the study period despite an overall downward trend in these proportions. Additional studies are needed to better understand the unique drivers of higher prescribing practices for ARI in rural settings, where approximately 80 more inappropriate antibiotics per 1000 person-years are prescribed compared with urban settings.

Strengths of our study include a robust database with a large sample of children followed over time. Comprehensive, longitudinal follow-up afforded calculation of incidence rates of ARI, ARI-related antibiotic use, and ARI-related inappropriate antibiotic use. Although many studies have assessed pediatric antibiotic use, our study is one of few to address “inappropriate” antibiotic use in children. In addition, our study focused on an important but understudied population. Children enrolled in Medicaid are disproportionately underrepresented in research but contribute to approximately half of the pediatric population in Tennessee and a similar proportion in many other states [8, 16, 44].

Our study also has some limitations, including reliance on diagnosis codes, which may not accurately or comprehensively reflect patients’ conditions or providers’ reasoning for prescribing antibiotics. In one review of the use of ICD-9 codes for inpatient diagnosis of community-acquired pneumonia, the positive predictive value ranged from 68% to 90% [45]; however, the performance of ICD codes to identify outpatient ARI is less clear. This misclassification would likely make it more difficult for our study to demonstrate differences between exposure groups. Another potential misclassification is our definition of rurality, which does not account for potential overlap in rurality level within individual counties, particularly in MR counties, which the US Census Bureau defines as those with 50%–99.9% of the population living in rural counties. In our study, we did not measure rates of non-ARI diagnoses or non-antibiotic prescriptions; future studies examining rates of other diagnoses and prescriptions during this time period can help elucidate whether overall coding of both ARI and other non-ARI diagnoses and/or prescribing behaviors for non-antibiotic medications also declined. We also did not have access to rates of immunization based upon rurality of county. Although regional variation in the proportion of young children enrolled in TennCare who are fully immunized exists and ranges between 57% and 92% (as of 2017), whether their vaccine status is associated with antibiotic use is unclear [46]. We limited our designation of inappropriate antibiotic use to the use of any antibiotic for conditions in which antibiotics are not indicated [3], but we did not verify the appropriateness of antibiotic choice, dose, or duration. The appropriateness of use of specific antibiotics for each diagnostic condition was beyond the scope of this analysis, given that we did not have access to children’s antibiotic allergy information or microbiological profiles. In addition, some antibiotic use for tier 2 diagnoses (for which antibiotics are sometimes indicated) may be inappropriate, leading to further underestimation of rates of inappropriate antibiotic use. We did not have access to information on prescriber type or setting, both of which may be associated with patterns of antibiotic prescribing [18, 47]. Although we excluded many children who are at increased risk for infection

at antibiotic use, we did not exclude all children with complex chronic conditions [48] who may also be at higher risk for infection. Finally, the findings are limited to children enrolled in TennCare and may not be directly generalizable to other populations.

## CONCLUSIONS

Acute respiratory infection-related inappropriate antibiotic use is very common among young children enrolled in TennCare, although rates have decreased over time. Inappropriate antibiotic use is significantly higher in children who reside in rural counties compared with urban counties. These findings should inform targeted outpatient stewardship efforts to reduce inappropriate antibiotic use and its consequences.

## Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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**Author contributions.** K. L. D., L. M. H., and C. G. G. conceptualized and designed the study, conducted the analyses, drafted the initial manuscript, and reviewed and revised the manuscript. J. B. designed the data collection instruments, collected data, carried out the initial analyses, and reviewed and revised the manuscript. H. G. assisted with design of the study and data analyses and reviewed and revised the manuscript. K. M. E. and R. B. contributed to the design of the study, assisted with drafting on the initial manuscript, and critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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