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**ASSESSING AND COMPARING ANTIBIOTIC THERAPY TRENDS FOR CHILDREN
WITH ACUTE OTITIS MEDIA FROM 2005 TO 2014 IN U.S**

A Thesis in

Public Health Sciences

by

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Abstract

Background

Approximately 30% of antibiotics prescribed in the outpatient setting is unnecessary. The centers for Disease Control and Prevention (CDC) has identified a number of infectious diseases states that have been associated with inappropriate use of antibiotics, including acute otitis media (AOM). The objective of this study is to assess the variation in the rate of antibiotic prescribing for children with acute otitis media over time across the U.S.

Methods

We analyzed data from the Truven Health MarketScan® Research database. The database includes primarily commercial health insurance data submitted from 2005 through 2011. The study sample included all children under the age of 12 years old with an ICD-9 diagnosis for acute otitis media (382, 384.20, 384.29). The primary outcome is filling a prescription for an antibiotic medication. Rates of antibiotic prescribing were compared over time and across U.S. Census regions. Logistic regression was used to identify demographic (age and sex) and geographic (U.S. Census regions) factors associated with antibiotic use for AOM.

Results

A total of 6,764,655 children aged less than 12 years old with a diagnosis of acute otitis media were identified after eliminating children with any missing values. Overall, the mean age was 4.3 ± 3.2 years. The distribution of the sample by U.S. Census region was as follows: 15.6% (n=1,059,978) in the North region, 23.3% (n=1,577,475) in the Midwest region, 43.8% (n=2,959,741) in the South region and 17.3% (n=1,167,461) in the West region. Overall, 60.7% of AOM children received an antibiotic, with rates of antibiotic use being highest in the West (62.7%), followed by the Midwest (61.8%), the South (60.5%), and the North (57.4%).

Conclusion

Based on the results of this study, overall antibiotic usage for acute otitis media for children with under age of 12 appears to be stable over the past decade, although rates vary dramatically by U.S. Census region. This shows the inconsistency of practice among different regions and need for standardization for treatment of AOM.

Table of Contents

List of Tables.....	v
Introduction.....	1
Methods.....	3
Study Subjects.....	3
Data Structure.....	3
Statistical Analysis.....	4
Results.....	4
Descriptive Statistics.....	4
Discussion.....	5
Conclusions.....	8
Tables.....	9
References.....	16

List of Tables

Table 1. Descriptive statistics of baseline demographics.....	9
Figure 1. Prevalence of acute otitis media across years 2005-2014 for all children.....	10
Figure 2. Percent of patients getting antibiotics among years 2005-2014 among all regions.....	11
Figure 3. Average antibiotic use among children with acute otitis media years 2005-2014 among all regions.....	12
Figure 4. Percent of children received antibiotics for AOM diagnosis by age.....	13
Figure 5. Distribution of age among patients receiving antibiotics.....	14
Table 2. Logistic Regression model results.....	15

Introduction

According to the Centers for Disease Control and Prevention (CDC), \$10.7 billion was spent on antibiotics in the United States in 2009.¹ In addition, approximately 30% of antibiotics prescribed in the outpatient setting is unnecessary, since they are often used to treat infections (such as acute respiratory infections), caused mainly by viruses and some sinus and ear infections.^{1,4} Antibiotics are also the most common cause of adverse effects, especially in children, and one of leading causes of emergency department visits in children.¹⁻⁴ Overuse of antibiotics has been associated with increased antibiotic resistance in children and adults.¹

In 2007, the CDC launched an initiative called Get Smart: Know When Antibiotics Work to help combat the increasing problem of antibiotic resistance.¹ This initiative included implementation of programs and measurements on global, national, state and local levels.¹⁻³ The CDC has identified a number of infectious diseases states that have been associated with inappropriate use of antibiotics, including acute otitis media (AOM).¹ AOM is usually defined as presence of middle-ear effusion combined with rapid onset of various symptoms that are commonly associated with high morbidity but low mortality.⁴ Approximately 50% to 85% of children will experience at least one episode of AOM by age three.^{4,5} Antibiotics are commonly prescribed for AOM but may not necessarily be warranted. According to the latest Cochrane review, the rates for antibiotic therapy vary greatly across countries (56% in the Netherlands and 95% in U.S.A and Canada).⁶ This pattern is mainly due to the fact that there is currently no consensus on the use of antibiotics in AOM.⁶ Due to the ambiguous diagnosis of acute otitis media infections, many children receive unwarranted antibiotics.⁵ The updated

AOM guidelines from the American Academy of Pediatrics (AAP), recommends the use of antibiotics in AOM for the following cases: 1) children 6 months and older with severe signs (moderate or severe otalgia or otalgia for at least 48 hours or temperature 39°C or higher), or 2) children younger than 24 months with bilateral AOM without severe signs or symptoms (mild otalgia for less than 48 hours, temperature less than 39°C), or 3) for non-severe unilateral AOM, it is recommended to either observe with close follow-up or prescribe antibiotics in children 6 months to 23 months of age without severe signs or symptoms.⁵ Hence, for the following scenarios, the AAP guidelines recommend observation without antibiotic therapy: Bilateral AOM without otorrhea for children ≥ 2 years old and any child with unilateral AOM without otorrhea.⁵

Following the 2004 AAP guidelines update, a few studies assessed the variability in antibiotic prescribing patterns and showed no significant change in frequency of clinic visits due to AOM or change in prescribing patterns.^{6,7,10} However, there have not been studies reporting prescribing patterns following the 2013 AAP guidelines update. In 2013, McGrath et al. utilized health insurance data to assess trends in antibiotic prescribing across the U.S for AOM.⁹ Investigators reported the antibiotic prescribing pattern over 10-year period to remain high.⁹ However, McGrath et al. lacked assessment of geographical variation across U.S., which can be of benefit when assessing for areas for improvement in quality of care. To our knowledge, there has not been an evaluation assessing prescribing patterns for antibiotics among children with AOM across different geographical regions in the U.S. Evaluating the geographical pattern across U.S would be beneficial to assess overall treatment trends and consistency.

Thus, the objective of this study is to assess the variation of antibiotic prescribing for children under the age of 12 years old with acute otitis media over time across the U.S.

Methods

Study population

We analyzed data from the Truven Health MarketScan® Commercial Claim and Encounters database for the years 2005 through 2011. MarketScan includes commercial claims data consisting of patient-specific utilization, expenditures and other service-related data. The database includes information from employer-sponsored plans for active employees and early retirees. It provides information regarding: inpatient and outpatient services and admissions, prescription drugs (including fill dates and refill history), laboratory services, service and admission dates, diagnosis-related groups and International Classification of Diseases codes (ICD). The study sample included children under age 12 who had at least one claim with an associated ICD-9 code corresponding to AOM (382, 384.20, or 384.29). Children prescribed an antibiotic were identified as those children who had a prescription claim within seven days of the service date associated with the AOM claim. The following antibiotic classes were identified: aminoglycoside, cephalosporin, beta-lactams, penicillin, tetracycline, quinolones, sulfones and any miscellaneous antibiotics identified by system.

Outcomes

The primary outcome was the proportion of children with AOM who received an antibiotic. We examined rates of antibiotic use over time, both overall and by U.S.

Census region. Secondary outcomes included evaluating prevalence of AOM over time and variation in rates of antibiotic use among different age groups.

Statistical analysis

Descriptive statistics, means, standard deviations and proportions were used to describe the AOM sample. Chi-square and t-tests were used to compare baseline characteristics among the group that received antibiotics versus the group that did not. Overall antibiotic use was evaluated over the 10-year period among different Census regions and by age. Logistic regression was used to identify patient demographic (age and sex) and geographic (U.S. Census regions) factors associated with antibiotic use for AOM. Findings were considered statistically significant if the p-value was less than 0.05. Data were analyzed using the statistical program SAS version 9.4 (SAS Institute Inc., Cary, NC).

Results

There was a total of 6,764,655 children under age 12 years who were identified with an acute otitis media diagnosis after eliminating children with any missing values. Characteristics of the sample are presented in Table 1. Overall, the mean age was 4.3 ± 3.2 years. Patients receiving antibiotics were slightly older (4.5 ± 3.2 versus 4.2 ± 3.3 , $p < 0.0001$) and a slightly higher proportion was female (48.2% versus 47.7%, $p < 0.0001$). The distribution of study sample by region was as follows: 15.6% ($n=1,059,978$) in the North region, 23.3% ($n=1,577,475$) in the Midwest region, 43.8% ($n=2,959,741$) in the South region, and 17.3% ($n=1,167,461$) in the West region. The prevalence of AOM increased sharply from 6.1% to 10.8% between 2005 and 2008, flattened out between 2008 and 2010, reached a high of 12.6% in 2012, and then fell to 9.6% by 2014 (Figure

1). Rates of antibiotic use were highest in the West (62.7%), followed by the Midwest (61.8%), the South (60.5%), and the North (57.4%). Across all regions, rates of antibiotic use from 2005 through 2014 ranged from 57.8% to 66% (Figure 2). Changes over time in antibiotic use did not vary considerably across the four Census regions (Figure 3). Although rates of antibiotic use were slightly lower among children aged 2 and under, the changes in the rates of antibiotic use in this group over time was similar to the pattern seen in children over age 2 (Figure 4). We found that children between ages 1 and 5 to receive more antibiotics for AOM compared between ages >5 to 12 years old (Figure 5). In multivariate logistic regression modeling, independent predictors of children receiving an antibiotic for AOM are shown in Table 2. Compared to the West, the likelihood of children receiving an antibiotic were lowest in the North region (OR 0.79, 95%CI [0.78 – 0.79]), followed by the South region (OR 0.89, 95%CI [0.88 – 0.89]) and the Midwest region (OR 0.93, 95%CI [0.92 – 0.93]). Although statistically significant, the effects of age, gender and year on the likelihood of receiving an antibiotic were much smaller compared to Census region (Table 2).

Discussion

We assessed the variation of antibiotic prescribing for children under the age of 12 years old with acute otitis media over time across U.S. We found that the prevalence of AOM was higher in females versus males in our study population. The rates of antibiotic use across all regions ranged from 57.8% to 66.1% between 2005 and 2014. Rates of antibiotic use were highest in the West (62.7%), followed by the Midwest (61.8%), the South (60.5%), and the North (57.4%). There was no significant change in prevalence of AOM across years for different age groups (less than and older than 2

years old). The distribution of females and males were almost even among overall population diagnosed with AOM and children receiving antibiotics for AOM which is interesting since AOM is more prevalent in males.¹³

AOM is a highly prevalent condition for which antibiotics are commonly prescribed.⁵ The trend of prevalence of disease from 2005 to 2014 followed an interesting pattern, where the rates of children with AOM was steadily increased from 2005 to 2008, plateaued from 2008 to 2010, increased from 2010 to 2012, and then declined sharply from 2012 to 2013. Our results conflict with McGrath et al; they reported a decline in AOM cases as well as antibiotic use following 2004 AAP guidelines.⁸ However, the decrease in AOM did not last since they reported a high rate of antibiotic utilization from 2007 until 2011, which is more consistent with our data. A major issue with the 2004 AOM AAP guidelines, is the lack of a defined diagnosis of AOM. This has resulted in over-utilization of antibiotics and diagnosis of AOM cases in children where watchful waiting or cases of acute otitis media with effusion (where no antibiotics are indicated) may have been more appropriate. The updated 2013 AOM AAP guidelines provided more accurate diagnosis for AOM with recommendations for specific scenarios for antibiotic use⁵. To our knowledge, there has not been any reported data to assess changes in prescribing patterns following the guideline update. Our data does not show any change from 2013 to 2014 in percent of children diagnosed with AOM nor those receiving antibiotics.

For children less than age 2, there was a 10% decrease in antibiotics use compared to children above age 2. This could have been due to lack of explicit

description of symptoms from preverbal younger children, hence resulting in more over-treating due to inability to rule out possible AOM versus other infectious etiologies.

Clinic visits for AOM decreased from 1995 to 2006 from 950 to 634 per 1000 children.⁵ This decrease in clinic visits has thus correlated with decreased antibiotic prescriptions for AOM from 1995 to 2006 resulting in relatively stable rate at 80% in 1995-1996 to 76% in 2005-2006.⁵ In our study, we report similar results, where the average rates of antibiotic use remained fairly stable from 2005 through 2014 at 62.4%. Based on these data, there has been a roughly 10% decrease in percentage of antibiotic therapy for AOM every 10 years in U.S. from 1995 to 2014 (80% in 1995-1996, to 76% in 2005 to 2006, to 62.4% in 2014). Despite the overall trend towards decreasing prescribing of antibiotics for AOM, we did find variation among different regions in U.S. We found that the highest rates of antibiotic prescribing were in the West and Midwest regions.

The AAP published AOM treatment guidelines in 2004 and updated them in 2013. Five years following the 2004 guidelines update, Coco et al. found no change in treatment patterns for AOM.^{7,9} One would expect an increase in average antibiotic usage for AOM after 2004 due to permissible use of antibiotics in cases that may not warrant antibiotic therapy. However, based on overall averages reported there was a downward trend from 1995 to 2014.⁷ The 2013 AAP AOM update provided more stringent guidelines for diagnosis and management of AOM. In our study, we observed an overall lower average of antibiotic use for AOM compared to previous years. However, it would be difficult to extrapolate or attribute the decrease to the AAP guideline update.

There were several limitations in this study. First, the claims data lack clinical factors such as severity of illness, temperature readings and presence of signs and symptoms of AOM infection. This could have potentially provided a better understanding of the patient population evaluated. Second, we did not have information on patients' family history to assess for predisposition for AOM in certain children. Third, due to the nature of the database, we are not able to confirm the diagnosis of AOM due to possibility of coding error. Finally, while we were able to correlate antibiotic prescribed to the service date of AOM episode encounter, we cannot guarantee that the antibiotic was intended to treat AOM as opposed to another co-infection.

Conclusion

Based on this study, it is apparent that while the overall rates of antibiotic utilization are stable, there is variation in antibiotic utilization across regions of U.S. for AOM in children under age 12. This calls for more standardization in clinical approaches to treating AOM. Also, further studies are needed to assess the impact of the recently updated AAP guidelines.

Tables

Table 1. Baseline demographics

Characteristic	Total sample n=6,764,655	Patients receiving NOT antibiotics n=2,657,241	Patients receiving antibiotics n=4,107,414	P-value
Age (Mean±SD), years	4.34±3.24	4.2±3.3	4.5±3.2	<0.0001
Sex, n(%) Female	3,245,402 (47.9)	1,268, 474(47.7)	1,977,928 (48.2)	<0.0001
Region				
<i>North</i>	1,059,978 (15.6)	451,108 (42.5)	608,870 (57)	<0.0001
<i>Midwest</i>	1,577,475 (23.3)	602,650 (38)	974,825 (61.8)	
<i>South</i>	2,959,741 (43.8)	1,168,155 (39)	1,791,586 (60.5)	
<i>West</i>	1,167,461 (17.3)	435,328 (37)	732,133 (62.7)	

Figure 1. Prevalence of acute otitis media across years 2005-2014 for all children

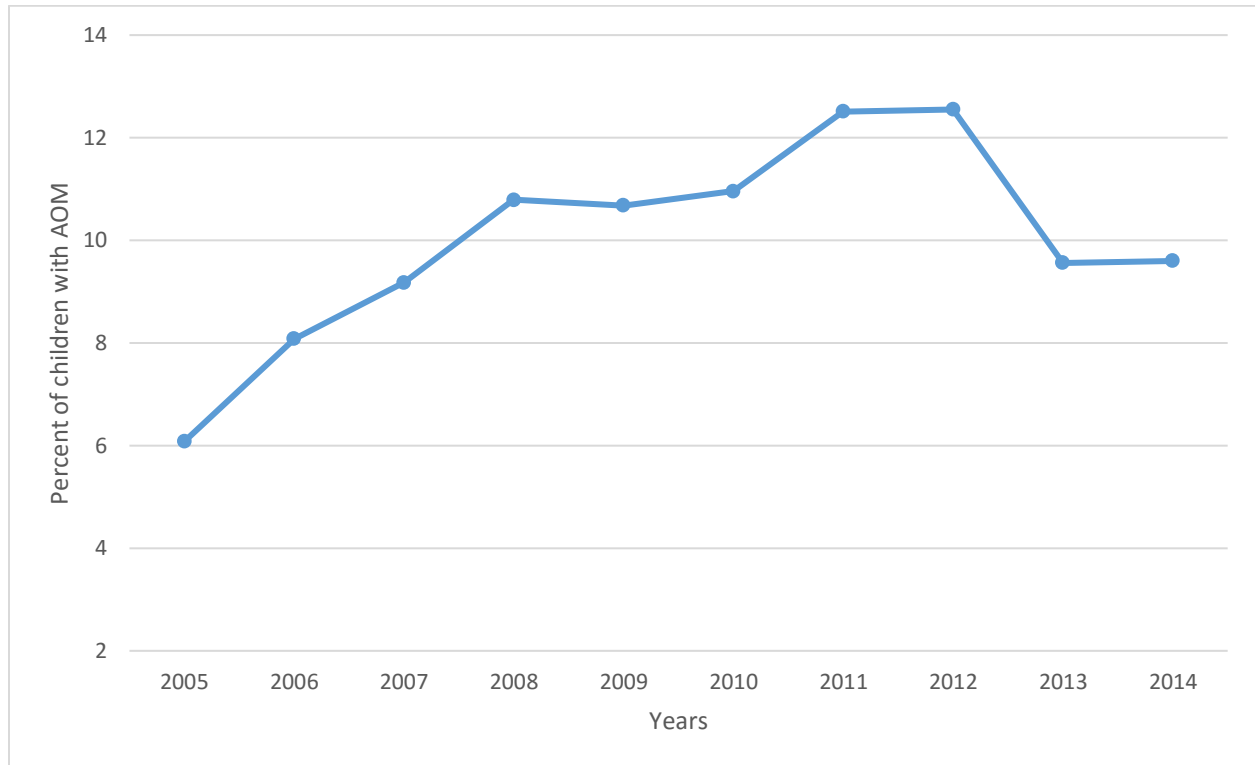


Figure 2. Percent of patients getting antibiotics among years 2005- 2014

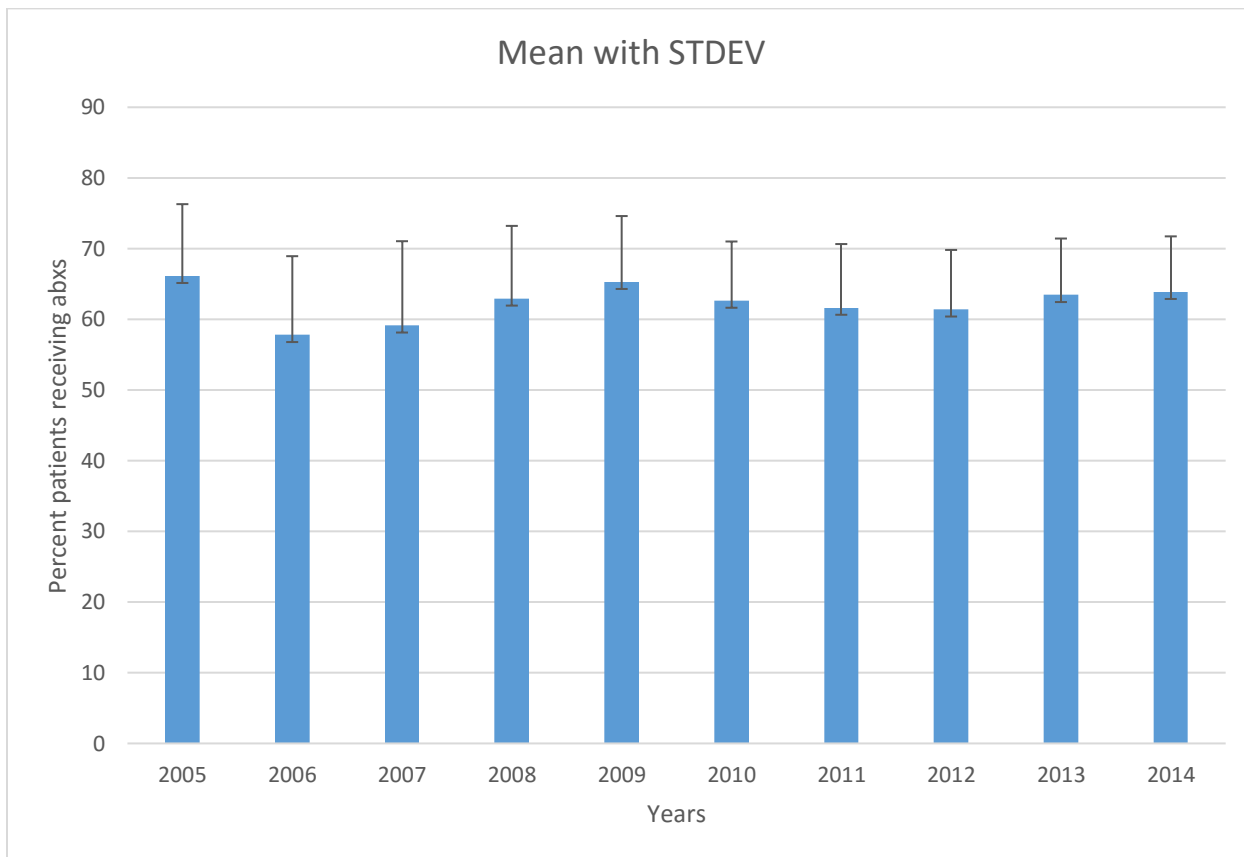


Figure 3. Average antibiotic use among children with acute otitis media years 2005-2014 among all regions

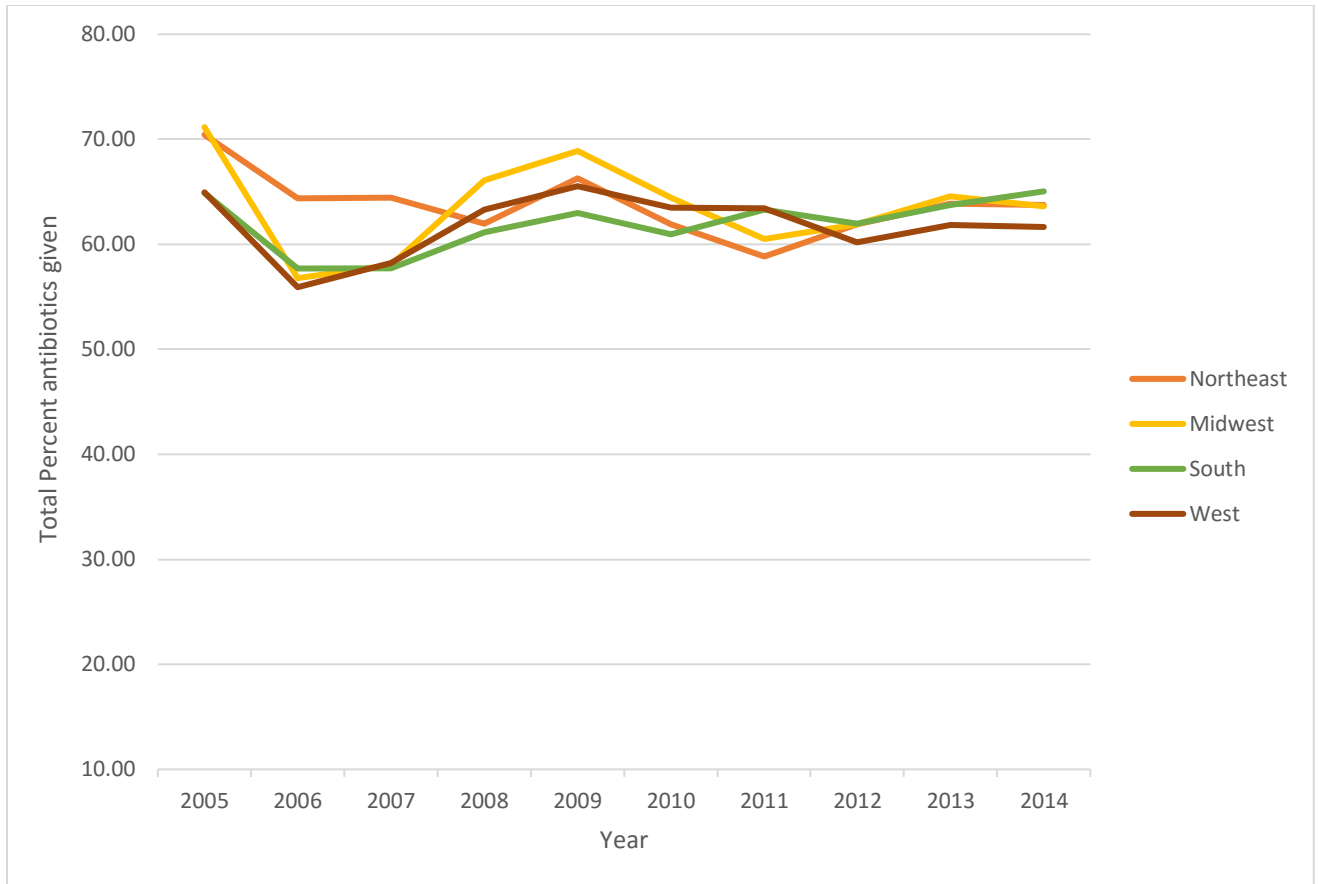


Figure 4. Percent of children received antibiotics for AOM diagnosis by age

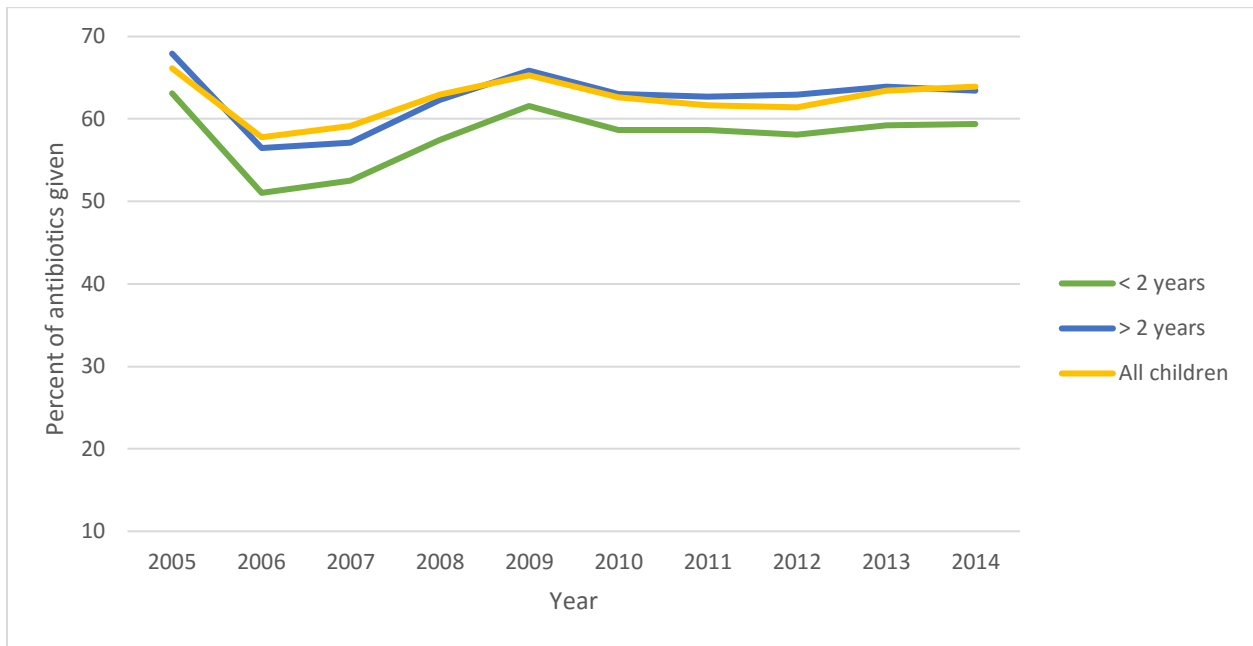


Figure 5. Distribution of age among patients receiving antibiotics

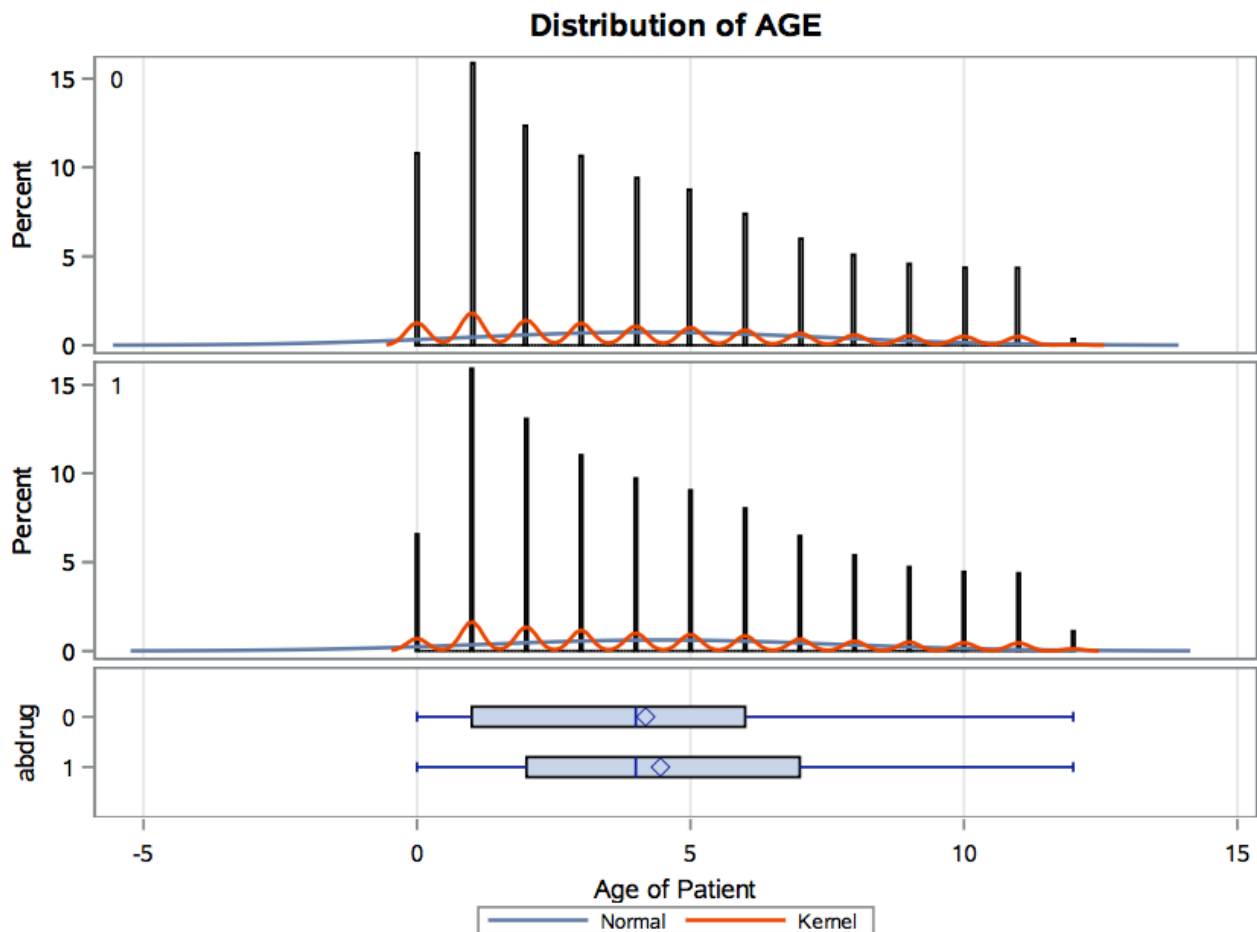


Table 2. Logistic regression model

Variable	Odds Ratio	95% Confidence Interval
Age	1.024	1.023 - 1.024
Sex (female)	1.014	1.01 – 1.02
Regions		
<i>North</i>	0.79	0.78 – 0.79
<i>Midwest</i>	0.93	0.92 – 0.93
<i>South</i>	0.89	0.88 – 0.89
<i>West</i>	Reference	Reference
Year	1.016	1.015 – 1.016

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