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Factors Associated with Antibiotic Misuse in Outpatient Treatment for Upper Respiratory Tract Infections

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The Centers for Disease Control and Prevention has promoted the appropriate use of antibiotics since 1995 when it initiated the National Campaign for Appropriate Antibiotic Use in the Community. This study examined upper respiratory tract infections included in the campaign to determine the degree to which antibiotics were appropriately prescribed and subsequent admission rates in a veteran population. This study was a retrospective chart review conducted among outpatients with a diagnosis of a respiratory tract infection, including bronchitis, pharyngitis, sinusitis, or nonspecific upper respiratory tract infection, between January 2009 and December 2011. The study found that 595 (35.8%) patients were treated appropriately, and 1,067 (64.2%) patients received therapy considered inappropriate based on the Get Smart Campaign criteria. Overall the subsequent readmission rate was 1.5%. The majority (77.5%) of patients were prescribed an antibiotic. The most common antibiotics prescribed were azithromycin (39.0%), amoxicillin-clavulanate (13.2%), and moxifloxacin (7.5%). A multivariate regression analysis demonstrated significant predictors of appropriate treatment, including the presence of tonsillar exudates (odds ratio [OR], 0.6; confidence interval [CI], 0.3 to 0.9), fever (OR, 0.6; CI, 0.4 to 0.9), and lymphadenopathy (OR, 0.4; CI, 0.3 to 0.6), while penicillin allergy (OR, 2.9; CI, 1.7 to 4.7) and cough (OR, 1.6; CI, 1.1 to 2.2) were significant predictors for inappropriate treatment. Poor compliance with the Get Smart Campaign was found in outpatients for respiratory infections. Results from this study demonstrate the overprescribing of antibiotics, while providing a focused view of improper prescribing. This article provides evidence that current efforts are insufficient for curtailing inappropriate antibiotic use.

The Centers for Disease Control and Prevention (CDC) has promoted the appropriate use of antibiotics since 1995 when it initiated the National Campaign for Appropriate Antibiotic Use in the Community (1). In 2003, this program was renamed Get Smart: Know When Antibiotics Work in conjunction with the launch of a national media campaign. The purpose of this campaign was to curb the rise of antimicrobial resistance, which has been deemed a hazard to public health by groups such as the Institute of Medicine (1, 2). Antibiotic prescribing rates for upper respiratory infections (URIs) alarmingly account for three-quarters of all antibiotic prescriptions written by office-based prescribers (1). There are many different symptoms of respiratory illnesses that bring patients to seek medical attention in the outpatient setting. Cough, congestion, fever, chills, nasal discharge, and sputum production are common symptoms of URIs, most of which are self-limiting and viral in origin (3–6). As part of the Get Smart Campaign, the CDC provides diagnostic criteria and prescribing guidelines for URIs (1).

This study examines URIs included in the CDC's Get Smart Campaign to determine the degree to which antibiotics were appropriately prescribed in an outpatient veteran population. It also aims to determine symptoms associated with inappropriate treatment and subsequent admission rates. Other published studies were limited by the use of quantities of antibiotics used but were unable to utilize patient specific data, such as diagnoses and patient visits (7). Bronchitis, pharyngitis, sinusitis, and nonspecific upper respiratory infections were included to determine appropriateness of treatment per the Get Smart Campaign recommendations (8–11).

MATERIALS AND METHODS

Study design. This study was a retrospective chart review conducted among adult patients who had a diagnosis of a respiratory tract infection. Respiratory tract infections were identified by *International Classification of Diseases*, *Ninth Revision* (ICD-9) codes with each respiratory diagnosis, including nonspecific URI, acute bronchitis, pharyngitis, and sinusitis. ICD-9 codes used were 465.8, 465.9, 466, 472, 473, and 474. A randomized consecutive qualified sampling process was used to select patients from the veteran population who were seen in the Veterans Affairs Western New York Healthcare System (VAWNYHS) emergency room and primary care clinics between the dates of 1 January 2009 and 31 December 2011.

Patients were included in the study if they were 18 years of age or older and were treated in the outpatient setting for one of the respiratory illnesses listed above. Each patient was included in the study only once. There were no standard antimicrobial order sets at the institution during the time of this study.

Patients were excluded if they initially presented at non-VAWNYHS institutions (e.g., emergency department, hospital, or other health care clinic). Patients were also excluded from the study if they carried a diagnosis of HIV/AIDs, were on chronic immunosuppressants, such as methotrexate, prednisone, or antitumor necrosis factor treatments, or were receiving active chemotherapy or any form of dialysis. These patients were excluded because the Get Smart Campaign applies to "otherwise healthy adults" (1). Patient symptoms, labs, and other characteristics were re-

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viewed to determine if the patient's clinical presentation coincided with diagnosis. If diagnosis did not match clinical presentation (i.e., incorrect ICD-9 chosen), the patient was then excluded from the study.

The Veterans Affairs (VA) Computerized Patient Record System (CPRS) was used to gather the information, and the Vista FileMan program was used to extract data using the ICD-9 codes listed above. Baseline demographics collected included age, sex, race, serum creatinine, weight, smoking status, diagnosis of respiratory tract infection, symptoms, and whether or not antibiotics were prescribed. Additional data collected included comorbid conditions, including heart failure (HF), chronic obstructive pulmonary disease (COPD), asthma, and diabetes. Outcome data also included admission of the patient, due to any cause, within 30 days of the clinical encounter and if the patient later developed *Clostridium difficile* infection (CDI). Appropriate antibiotic prescribing and diagnostics were evaluated based on the CDC's recommendations from the Get Smart Campaign.

Definitions. Appropriate treatment was evaluated based on the following definitions from the CDC's Get Smart Campaign.

(i) Bronchitis. Cough was the dominant complaint for diagnosis of bronchitis, and pneumonia was ruled out in all cases with chest X-ray. Appropriate treatment was classified as symptomatic care with no antibiotic prescribed (9).

(ii) Pharyngitis. Sudden onset of symptoms, including sore throat, inflammation of pharynx and tonsils, and patchy, discrete exudates, was the diagnostic criterion for pharyngitis (11). Treatment was considered appropriate if the patient had at least 2 of the following 4 criteria: history of fever, no cough, tonsillar exudates, or tender anterior cervical adenopathy. The rapid strep test was not used, as the VA did not obtain this test until 2011. Patients were appropriately treated if penicillin, amoxicillin, a 1st- or 2nd-generation cephalosporin, or a macrolide in penicillin-allergic patients was used.

(iii) Sinusitis. Severe symptoms, including high fever (a temperature of >39°C [102°F]) and purulent nasal discharge or facial pain lasting for at least 3 to 4 consecutive days, were used to define appropriateness of antibiotic prescription. Appropriate first-line treatment was amoxicillin-clavulanate or doxycycline (1, 12). Amoxicillin was also considered appropriate based on the time period studied (1, 10). Doxycycline or a respiratory fluoroquinolone (levofloxacin or moxifloxacin) was an appropriate alternative for penicillin-allergic patients (1, 12).

(iv) Nonspecific upper respiratory tract infection. Symptoms included sore throat, nasal symptoms, and cough; however, there was no prominent symptom or sign to indicate a bacterial infection. Appropriate treatment was defined as symptomatic care with no antibiotic prescribed (8).

Statistical analysis. The primary objective of this study was to evaluate the appropriateness of antibiotic therapy in the outpatient setting for patients being treated for respiratory illnesses in conjunction with the Get Smart Campaign. Bivariate analysis was used to compare those treated appropriately versus those inappropriately treated by using the independent sample *t* test for continuous variables and either the chi-squared or Fisher's exact test for categorical variables to evaluate significant differences with respect to baseline characteristics.

The secondary objective was to determine the factors that contribute to antibiotic prescription for any upper respiratory-type infection. Aggregate significant baseline characteristics and symptomatology ($P < 0.05$) from the bivariate analysis were built into a multivariate logistic regression analysis to determine predictors of appropriate treatment. Factors were eliminated in a backwards elimination fashion until a stable model for predicting antibiotic use in the outpatient setting was achieved. Results are presented as odds ratios (ORs) with 95% confidence intervals (CIs).

Admission rates with and without appropriate treatment and antibiotic use are presented with descriptive statistics as well as ORs with 95% CIs. Admission rates were also calculated for COPD patients, as this is a particularly vulnerable population.

RESULTS

This study included 1,662 veterans treated for a respiratory infection described in the Get Smart Campaign. For the indications of sinusitis, bronchitis, nonspecific URI, and pharyngitis examined in this study, 595 (35.8%) patients were treated appropriately, and 1,067 (64.2%) patients received therapy considered inappropriate based on the Get Smart Campaign criteria (Table 1). The majority (77.5%) of patients were prescribed an antibiotic. The most common antibiotics prescribed were azithromycin (39.0%), moxifloxacin (7.5%), and amoxicillin-clavulanate (13.2%). When examined by antibiotic class, 39.6% received a macrolide, 27.0% a penicillin, 8.1% a fluoroquinolone, and 1.5% a cephalosporin.

Bronchitis was treated appropriately in 20.5% of cases; in those inappropriately treated, 1.6% had a subsequent admission within 30 days. In those appropriately treated with symptomatic care, 1.2% had a subsequent admission within 30 days ($P = 0.8$). A macrolide was most commonly prescribed for bronchitis (70.1%). Pharyngitis was treated appropriately in 39.3% of cases. The most common antibiotic prescribed was penicillin. The majority of the inappropriately treated patients (94.3%) received antibiotics when it was not indicated (Table 2). Of patients treated appropriately, 1.9% had admission within 30 days compared with 0.4% of those inappropriately treated ($P = 0.1$). Sinusitis was treated appropriately in 43.8% of patients. The most common antibiotic class prescribed was the penicillin class. The majority of the inappropriately treated patients (52.0%) received antibiotics when it was not indicated (Table 2). Symptomatic/supportive treatment was given to 71.0% of the sinusitis population. Of patients treated appropriately, 1.7% had admission within 30 days compared with 0.9% of those inappropriately treated ($P = 0.5$). Nonspecific URIs were treated appropriately in 30.3% of patients. Of patients treated appropriately, 1.7% had admission within 30 days compared with 2.5% of those inappropriately treated ($P = 0.5$). The most common antibiotic prescribed was a macrolide.

A bivariate analysis was performed, including the entire cohort to determine which factors may lead to inappropriate antibiotic prescription (Tables 1 and 3). On average, the age of those who received inappropriate therapy was 53.7 ± 16.3 years, while those patients who received appropriate therapy were slightly younger at 52.0 ± 17.5 years of age ($P = 0.04$). Patients with COPD also were more likely to receive inappropriate treatment ($P = 0.04$). Penicillin-allergic patents were more likely to receive inappropriate treatment ($P = 0.0003$). Baseline characteristics, including weight, sex, race, smoking status, heart failure, asthma, and diabetes, were not clinically significantly different between the two groups. Symptoms that were most associated with appropriate treatment in the bivariate analysis included the presence of fever ($P < 0.0001$), tonsillar exudates ($P = 0.001$), and lymphadenopathy ($P < 0.0001$). The presence of cough was more associated with inappropriate treatment ($P < 0.0001$) (Table 3).

A backward stepwise multivariate logistic regression analysis was used to remove the regressor that affects the fit of the model predicting inappropriate treatment the least. COPD was eliminated first ($P = 0.97$). Next, age ($P = 0.7$) and then indication ($P = 0.09$) were removed via backwards elimination. The final model was well fitted ($P < 0.0001$) to predict inappropriate treatment for respiratory infections. Significant predictors of appropriate treatment included presence of tonsillar exudates (OR, 0.6;

TABLE 1 Composite characteristics of patient cohort[a]

Parameter	Total cohort (n = 1,662)	Inappropriate treatment (n = 1,067)	Appropriate treatment (n = 595)	P value
Age (yr)	53.09 ± 16.72	53.72 ± 16.26	51.96 ± 17.47	0.039
Serum creatinine (mg/dl)	1.02 ± 0.28	1.03 ± 0.30	1.013 ± 0.24	0.27
Weight (kg)	92.48 ± 20.96	93.21 ± 21.09	91.26 ± 20.69	0.076
Sex (male)	81.65 (1,357)	82.29 (878)	80.5 (476)	0.37
Race				0.41
African American	22.08 (367)	21.65 (231)	22.86 (136)	
Other	4.75 (79)	4.31 (46)	5.55 (33)	
Caucasian	73.16 (1,216)	74.04 (790)	71.60 (426)	
Smoker	30.20 (502)	30.46 (325)	29.75 (177)	0.76
Heart failure	3.13 (52)	3.66 (39)	2.19 (13)	0.99
COPD	12.33 (205)	13.5 (145)	10.08 (60)	0.037
Asthma	7.64 (127)	7.69 (82)	7.56 (42)	0.93
Diabetes	22.86 (380)	23.90 (255)	21.01 (125)	0.18
Penicillin allergy	12.59 (101)	16.2 (76)	7.51 (25)	0.0003
Indication				<0.0001
Bronchitis	24.07 (400)	29.80 (318)	13.78 (82)	
Nonspecific URI	27.68 (460)	26.24 (280)	30.25 (180)	
Pharyngitis	24.19 (402)	22.87 (244)	26.55 (158)	
Sinusitis	24.07 (400)	21.09 (225)	29.41 (175)	
Drug class				<0.0001
Cephalosporin	1.5 (25)	2.34 (25)	0	
Clindamycin	0.18 (3)	0.28 (3)	0	
Antiviral	0.06 (1)	0.09 (1)	0	
Fluoroquinolone	8.06 (134)	11.81 (126)	1.34 (8)	
Macrolide	39.59 (658)	61.01 (651)	1.18 (7)	
No antibiotic	22.44 (373)	0	62.69 (373)	
Penicillin class	27.02 (449)	22.87 (244)	34.45 (205)	
Sulfa class	0.78 (13)	1.22 (13)	0	
Tetracycline	0.36 (6)	0.37 (4)	0.34 (2)	
Supportive care	74.46 (895)	75.35 (593)	72.77 (302)	0.33
Admission within 30 days	25 (1.50)	15 (1.41)	10 (1.68)	0.66

[a] Values shown are mean ± SD or percent (number).

CI, 0.3 to 0.9), fever (OR, 0.6; CI, 0.4 to 0.9), and lymphadenopathy (OR, 0.4; CI, 0.3 to 0.6). Penicillin allergy (OR, 2.9; CI, 1.7 to 4.7) and cough (OR, 1.6; CI, 1.1 to 2.2) were significant predictors for inappropriate treatment (Table 4).

Admission rates were analyzed across all categories. Twenty-five patients (1.5%) were admitted within 30 days of their respiratory infection. Of the patients admitted, 60% had been inappropriately treated, and 40% had been appropriately treated. There was no statistically significant difference in rates (P = 0.66). Admission rates were also analyzed between those who received antibiotics and those who did not. Of the 25 patients admitted, 76% had received antibiotics and 24% did not (P = 0.86). The odds of avoiding admission were calculated for appropriateness of treatment (OR, 0.77; 95% CI, 0.28 to 2.72) and whether antibiotics were prescribed (OR, 0.88; 95% CI, 0.29 to 3.98).

COPD can be a difficult diagnosis, as the threshold for error is low and can lead to admission. The odds of avoiding admission were calculated for appropriateness of treatment (OR, 0.72; 95% CI, 0.26 to 2.54), whether antibiotics were prescribed (OR, 0.86; 95% CI, 0.24 to 3.39), and diagnosis of COPD (OR, 0.34; 95% CI, 0.15 to 0.90).

TABLE 2 Reasons for inappropriate treatment

Diagnosis	Received antibiotics when not indicated (no. [%])	Did not receive antibiotics when indicated (no. [%])	Prescribed incorrect antibiotic (no. [%])	Total no. inappropriate treatment
Pharyngitis (n = 402)	230 (94.3)	1 (0.4)	13 (5.3)	244
Sinusitis (n = 400)	117 (52.0)	0	108 (48.0)	225
Bronchitis (n = 400)	318 (100)	0	0	318
Nonspecific URI (n = 460)	280 (100)	0	0	280

TABLE 3 Symptoms associated with appropriate versus inappropriate treatment

Parameter	Total cohort (n = 1,662) (% [no.])	Inappropriate treatment (n = 1,067) (% [no.])	Appropriate treatment (n = 595) (% [no.])	P value
Fever	26.21 (315)	18.42 (145)	40.96 (170)	<0.0001
Cough	76.53 (1,272)	80.32 (857)	69.75 (415)	<0.0001
Tonsillar exudates	10.35 (83)	7.46 (35)	14.41 (48)	0.0014
Lymphadenopathy	45.39 (364)	34.54 (162)	60.66 (364)	<0.0001
Tachypnea (≥25 breaths/min)	0.5 (2)	0.63 (2)	0	0.47
Tachycardia (≥100 beats/min)	14.0 (56)	13.84 (12)	14.63 (12)	0.85
Nasal symptoms	63.04 (290)	63.21 (177)	62.78 (113)	0.92

DISCUSSION

The CDC estimates that more than half of all antibiotics are inappropriately prescribed annually, primarily for conditions likely caused by viruses (1, 4, 13). Some improvement, however, has been made as evidenced by data from 9 U.S. health insurance companies, which showed a decrease in antibiotic prescriptions in the years between 1996 and 2000. Furthermore, data from the National Ambulatory Medical care survey showed a decrease in the use of antibiotics for acute respiratory tract infections when comparing the years 1995 to 1996 and 2005 to 2006 (14). In 2010, 258 million courses of antibiotics were prescribed in the United States (7). Antibiotic usage is a major driving factor for increased antibiotic resistance (15, 16). Recently, a report linked four classes of antibiotics commonly prescribed for respiratory infections in the outpatient setting to an increased incidence of nonsusceptible pneumococcal isolates (16). Inappropriate antibiotic prescribing not only impacts bacterial resistance but also is associated with adverse reactions, such as the development of CDI (17–19).

Poor compliance with the Get Smart Campaign was found in outpatients seen in the emergency room or primary care for respiratory infections. Of patients included, 35.8% of patients received care commensurate with the Get Smart Campaign. The majority of patients in this study (77.5%) received antibiotics, most frequently a macrolide, followed by penicillin, fluoroquinolone, and finally a cephalosporin. Similar to other studies in the literature, the most commonly prescribed antibiotic for URI was azithromycin (7).

Our study showed that patients with bronchitis or nonspecific upper respiratory tract infection were more likely to receive inappropriate treatment. Providers may feel compelled to prescribe antibiotic therapy even if the treatment may be inappropriate. A recent study that interviewed 36 primary care providers in the United States found that reasons for noncompliance in antibiotic prescribing include the belief that nonrecommended antibiotics are more likely to cure infection, patient satisfaction concerns, and fear of complications (20).

Cough was the symptom most commonly associated with inappropriate antibiotic prescribing for upper respiratory tract infections in the Get Smart Campaign. The presence of tonsillar exudates, lymphadenopathy, and fever were all associated with appropriate antibiotic prescribing, likely because these symptoms predict the presence of group A *streptococcus* infection. Penicillin-allergic patients were less likely to receive appropriate treatment commensurately with the guidelines, indicating that better education or pathways are needed to ensure appropriate treatment in the patient population.

TABLE 4 Multivariate analysis for predictors of inappropriate treatment of infections of the Get Smart Campaign

Predictor	P value	OR	95% CI
Tonsillar exudates	0.023	0.56	0.54–0.92
Cough	0.007	1.59	1.13–2.23
Fever	0.007	0.55	0.36–0.85
Lymphadenopathy	<0.0001	0.43	0.29–0.64
Penicillin allergy	<0.0001	2.81	1.13–2.23

Our study found no difference in hospitalization rates for those receiving guideline-specific therapy compared with rates for those who were inappropriately treated. There was also no difference in hospitalization rates between those patients who received antibiotics regardless of whether or not they were appropriate. Even in COPD patients who have a higher likelihood of being admitted, symptomatic care without antibiotic use is not associated with increased rates of hospitalization in the bronchitis and nonspecific respiratory infection categories. This indicates that the fear of complications from not prescribing antibiotics may be unfounded.

There are many studies in the literature that demonstrate that there is over-prescribing of antibiotics in the outpatient setting; however, there is a gap in the literature evaluating the actual appropriateness of therapy for specific indications (3, 4, 7). This study provides a detailed accounting of antibiotic use for respiratory infection and factors that increase the odds for antibiotic prescription. Identification of specific symptoms triggering inappropriate treatment, with an understanding of the scope of antibiotic use in the outpatient setting, will help clinicians recognize target areas for improvement. Utilizing the results of this study, we can garner areas for increased education and perhaps the need for outpatient antimicrobial stewardship to curb inappropriate treatment (18).

There are limitations to this study. The largest is that there are no data validating the Get Smart Campaign's definition of inappropriate prescribing. This study was limited to veterans in the outpatient setting, so results may not be generalizable to the average adult population. Since this study was a retrospective chart review, assessing appropriateness of antibiotics was based on information documented in the patient's chart. It is possible that a patient may have had additional symptoms that would have altered appropriateness of antibiotic prescription. The study did not examine duration of treatment, which may also increase instances of inappropriate treatment either by excessively lengthy courses or courses of insufficient length to treat the infection. This study also excluded immunocompromised patients; however, it would be interesting to determine if overtreatment is more prominent in

this population. Lastly, readmission rates were relatively small, and larger populations may be studied in the future to confirm these results.

In conclusion, despite the CDC's best efforts with the Get Smart: Know When Antibiotics Work Campaign, there is frequently a lack of awareness and outside pressure increasing antibiotic use in the outpatient setting. There is a growing threat of antimicrobial resistance making it important to identify the scope of the problem and factors impacting antibiotic prescription. This study reinforces the existing literature documenting the overprescribing of antibiotics for URIs while providing a focused view of improper prescribing. Areas for education of practitioners indicate that patients with a cough are over treated with antibiotics, and better knowledge of treatment alternatives for penicillin-allergic patients is needed. However, education is insufficient. Educational programs have been in place since 2003, and this study confirms that antibiotics are still widely overprescribed. Hospitalization rates were not increased in patients where they were appropriately treated with symptomatic care and antibiotics were withheld. Expansion of stewardship programs or performance standards to the outpatient setting is necessary to combat excessive and inappropriate antibiotic use.

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REFERENCES

1. **Centers for Disease Control and Prevention.** 2013. Get Smart programs & observances. Centers for Disease Control and Prevention, Atlanta, GA. http://www.cdc.gov/getsmart/. Accessed 29 October 2014.
2. **Institute of Medicine.** 2003. Microbial threats to health: emergence, detection, and response. The National Academies Press, Washington, DC.
3. **Gonzales R, Malone DC, Maselli JH, Sande MA.** 2001. Excessive antibiotic use for acute respiratory infections in the United States. Clin Infect Dis **33:**757–762. http://dx.doi.org/10.1086/322627.
4. **Centers for Disease Control and Prevention (CDC).** 2011. Office-related antibiotic prescribing for persons aged ≤14 years–United States, 1993-1994 to 2007-2008. MMWR Morb Mortal Wkly Rep **60:**1153–1156.
5. **Logan JL, Yang J, Forrest G.** 2012. Outpatient antibiotic prescribing in a low-risk veteran population with acute respiratory symptoms. Hosp Pract **40:**75–80. http://dx.doi.org/10.3810/hp.2012.02.948.
6. **Gonzales R, Bartlett JG, Besser RE, Hickner JM, Hoffman JR, Sande MA, American Academy of Family Physicians, Infectious Diseases Society of America, Centers for Disease Control, American College of Physicians-American Society of Internal Medicine.** 2001. Principles of appropriate antibiotic use for treatment of nonspecific upper respiratory tract infections in adults: background. Ann Intern Med **134:**490–494. http://dx.doi.org/10.7326/0003-4819-134-6-200103200-00015.
7. **Hicks LA, Taylor TH, Jr, Hunkler RJ.** 2013. U.S. outpatient antibiotic prescribing, 2010. N Engl J Med **368:**1461–1462. http://dx.doi.org/10.1056/NEJMc1212055.
8. **Centers for Disease Control and Prevention.** 2009. Nonspecific upper respiratory tract infection: physician information sheet (adults). Centers for Disease Control and Prevention, Atlanta, GA. http://www.cdc.gov/getsmart/campaign-materials/info-sheets/adult-nurti.html. Accessed 29 October 2014.
9. **Centers for Disease Control and Prevention.** 2013. Bronchitis (chest cold). Centers for Disease Control and Prevention, Atlanta, GA. http://www.cdc.gov/getsmart/antibiotic-use/uri/bronchitis.html. Accessed 29 October 2014.
10. **Centers for Disease Control and Prevention.** 2009. Acute bacterial rhinosinusitis: physician information sheet (adults). Centers for Disease Control and Prevention, Atlanta, GA. http://www.cdc.gov/getsmart/campaign-materials/info-sheets/adult-acute-bact-rhino.html. Accessed 29 October 2014.
11. **Centers for Disease Control and Prevention.** 2013. Sore throat. Centers for Disease Control and Prevention, Atlanta, GA. http://www.cdc.gov/getsmart/antibiotic-use/URI/sore-throat.html. Accessed 29 October 2014.
12. **Chow AW, Benninger MS, Brook I, Brozek JL, Goldstein EJ, Hicks LA, Pankey GA, Seleznick M, Volturo G, Wald ER, File TM, Jr, Infectious Diseases Society of America.** 2012. IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. Clin Infect Dis **54:**e72–e112. http://dx.doi.org/10.1093/cid/cis370.
13. **Pichichero ME.** 2002. Dynamics of antibiotic prescribing for children. JAMA **287:**3133–3135. http://dx.doi.org/10.1001/jama.287.23.3133.
14. **Huttner B, Goossens H, Verheij T, Harbarth S, CHAMP consortium.** 2010. Characteristics and outcomes of public campaigns aimed at improving the use of antibiotics in outpatients in high-income countries. Lancet Infect Dis **10:**17–31. http://dx.doi.org/10.1016/S1473-3099(09)70305-6.
15. **Albrich WC, Monnet DL, Harbarth S.** 2004. Antibiotic selection pressure and resistance in *Streptococcus pneumoniae* and *Streptococcus pyogenes*. Emerg Infect Dis **10:**514–517. http://dx.doi.org/10.3201/eid1003.030252.
16. **Hicks LA, Chien YW, Taylor TH, Jr, Haber M, Klugman KP.** 2011. Outpatient antibiotic prescribing and nonsusceptible *Streptococcus pneumoniae* in the United States, 1996-2003. Clin Infect Dis **53:**631–639. http://dx.doi.org/10.1093/cid/cir443.
17. **Aspinall SL, Metlay JP, Maselli JH, Gonzales R.** 2007. Impact of hospital formularies on fluoroquinolone prescribing in emergency departments. Am J Manag Care **13:**241–248.
18. **Muto CA, Pokrywka M, Shutt K, Mendelsohn AB, Nouri K, Posey K, Roberts T, Croyle K, Krystofiak S, Patel-Brown S, Pasculle AW, Paterson DL, Saul M, Harrison LH.** 2005. A large outbreak of *Clostridium difficile*-associated disease with an unexpected proportion of deaths and colectomies at a teaching hospital following increased fluoroquinolone use. Infect Control Hosp Epidemiol **26:**273–280. http://dx.doi.org/10.1086/502539.
19. **Neuhauser MM, Weinstein RA, Rydman R, Danziger LH, Karam G, Quinn JP.** 2003. Antibiotic resistance among gram-negative bacilli in US intensive care units: implications for fluoroquinolone use. JAMA **289:**885–888. http://dx.doi.org/10.1001/jama.289.7.885.
20. **Sanchez GV, Roberts RM, Albert AP, Johnson DD, Hicks LA.** 2014. Effects of knowledge, attitudes, and practices of primary care providers on antibiotic selection, United States. Emerg Infect Dis **20:**2041–2047. http://dx.doi.org/10.3201/eid2012.140331.