Original Investigation

Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-2011

Katherine E. Fleming-Dutra, MD; Adam L. Hersh, MD, PhD; Daniel J. Shapiro; Monina Bartoces, PhD; Eva A. Enns, PhD; Thomas M. File Jr, MD; Jonathan A. Finkelstein, MD, MPH; Jeffrey S. Gerber, MD, PhD; David Y. Hyun, MD; Jeffrey A. Linder, MD, MPH; Ruth Lynfield, MD; David J. Margolis, MD, PhD; Larissa S. May, MD, MSPH; Daniel Merenstein, MD; Joshua P. Metlay, MD, PhD; Jason G. Newland, MD, MEd; Jay F. Piccirillo, MD; Rebecca M. Roberts, MS; Guillermo V. Sanchez, MPH, PA-C; Katie J. Suda, PharmD, MS; Ann Thomas, MD, MPH; Teri Moser Woo, PhD; Rachel M. Zetts; Lauri A. Hicks, DO

IMPORTANCE The National Action Plan for Combating Antibiotic-Resistant Bacteria set a goal of reducing inappropriate outpatient antibiotic use by 50% by 2020, but the extent of inappropriate outpatient antibiotic use is unknown.

OBJECTIVE To estimate the rates of outpatient oral antibiotic prescribing by age and diagnosis, and the estimated portions of antibiotic use that may be inappropriate in adults and children in the United States.

DESIGN, SETTING, AND PARTICIPANTS Using the 2010-2011 National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey, annual numbers and population-adjusted rates with 95% confidence intervals of ambulatory visits with oral antibiotic prescriptions by age, region, and diagnosis in the United States were estimated.

EXPOSURES Ambulatory care visits.

MAIN OUTCOMES AND MEASURES Based on national guidelines and regional variation in prescribing, diagnosis-specific prevalence and rates of total and appropriate antibiotic prescriptions were determined. These rates were combined to calculate an estimate of the appropriate annual rate of antibiotic prescriptions per 1000 population.

RESULTS Of the 184 032 sampled visits, 12.6% of visits (95% CI, 12.0%-13.3%) resulted in antibiotic prescriptions. Sinusitis was the single diagnosis associated with the most antibiotic prescriptions per 1000 population (56 antibiotic prescriptions [95% CI, 48-64]), followed by suppurative otitis media (47 antibiotic prescriptions [95% CI, 41-54]), and pharyngitis (43 antibiotic prescriptions [95% CI, 38-49]). Collectively, acute respiratory conditions per 1000 population led to 221 antibiotic prescriptions (95% CI, 198-245) annually, but only 111 antibiotic prescriptions were estimated to be appropriate for these conditions. Per 1000 population, among all conditions and ages combined in 2010-2011, an estimated 506 antibiotic prescriptions (95% CI, 458-554) were written annually, and, of these, 353 antibiotic prescriptions were estimated to be appropriate antibiotic prescriptions.

CONCLUSIONS AND RELEVANCE In the United States in 2010-2011, there was an estimated annual antibiotic prescription rate per 1000 population of 506, but only an estimated 353 antibiotic prescriptions were likely appropriate, supporting the need for establishing a goal for outpatient antibiotic stewardship.

Editorial page 1839

Supplemental content at jama.com

CME Quiz at jamanetworkcme.com

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Katherine E. Fleming-Dutra, MD, Centers for Disease Control and Prevention, 1600 Clifton Rd, MS A-31, Atlanta, GA 30329-4027 (ftu2@cdc.gov).

JAMA. 2016;315(17):1864-1873. doi:10.1001/jama.2016.4151

Copyright 2016 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ by Arnab Mukherjee on 03/09/2020

Antibiotic-resistant infections affect 2 million people and are associated with 23 000 deaths annually in the United States, according to the Centers for Disease Control and Prevention (CDC).[1] Antibiotic use is the primary driver of antibiotic resistance[1] and leads to adverse events ranging from allergic reactions to *Clostridium difficile* infections.[2] Data from other developed nations suggest that 80% or more of antibiotic use (excluding agricultural use) occurs among outpatients.[3] In the United States in 2011, 262 million outpatient antibiotic prescriptions were dispensed.[4] Declining trends in antibiotic prescribing in the United States occurred in the 1990s and early 2000s but stabilized by 2010.[5,6]

Reducing inappropriate use is essential to reduce both antibiotic resistance and adverse events. National guidelines addressing when to prescribe antibiotics have been published over the last 2 decades for many common diagnoses.[7-10] The CDC's Get Smart: Know When Antibiotics Work program focuses on promoting appropriate outpatient antibiotic use.[11] In March 2015, the White House released the National Action Plan for Combating Antibiotic-Resistant Bacteria, which set a target of reducing inappropriate antibiotic use in the outpatient setting by 50% by 2020.[12] However, the fraction of antibiotic use that is inappropriate and amenable to reduction is unknown.[13] Previous goals and national measures of appropriate antibiotic use (eg, Healthy People 2020 targets and Healthcare Effectiveness Data and Information Set [HEDIS] measures) have targeted specific age groups and conditions (eg, ear infections or acute bronchitis).[14,15] To our knowledge, there is no current overall estimate of appropriate outpatient antibiotic prescribing that considers all ages and conditions that may receive antibiotics. The objectives of this study were to establish a baseline of the current rate of outpatient, oral antibiotic prescriptions by age and diagnosis and to estimate the overall rate of appropriate, outpatient antibiotic prescriptions in the United States to inform public health and antibiotic stewardship efforts.

Methods

Data Sources

Baseline antibiotic prescribing rates were estimated using the National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS). These cross-sectional surveys are administered annually by the CDC's National Center for Health Statistics.[16] NAMCS samples visits to nonfederally-employed, office-based physicians primarily engaged in patient care and selects visits using a 3-stage probability sampling design. NAMCS samples geographic regions, physicians, and visits during randomly assigned 1-week reporting periods. NHAMCS is a survey of emergency departments and outpatient departments of nonfederal general and short-stay hospitals.[16] NHAMCS uses a 4-stage probability sampling design. NHAMCS samples geographic regions, hospitals, outpatient department clinics, and emergency service areas, and visits during 4-week reporting periods. Data collected include patient demographics, up to 3 diagnoses that are coded by NAMCS/NHAMCS staff using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*), and up to 8 medications mentioned—meaning prescribed, continued, or provided at the visit.

Sampled visits in both surveys are distributed randomly throughout the year. Weights are assigned to visits so national estimates can be produced. The most recent 2 years of data available in both NAMCS and NHAMCS (2010-2011) were used. Unweighted response rates during 2010-2011 ranged from 54.1% to 58.3% for physicians in NAMCS, 66.7% to 73.6% for outpatient departments, and 80.4% to 87.5% for emergency departments in NHAMCS. Estimates from NAMCS are adjusted for physician and item nonresponse. Estimates from NHAMCS are adjusted for hospital nonresponse and for nonresponse at the level of the emergency departments and outpatient departments. The National Center for Health Statistics research ethics review board approved NAMCS/NHAMCS, with waivers of informed consent and Health Insurance Portability and Accountability Act authorization for patients. These analyses were based on publically available, deidentified data, and therefore were not subject to institutional review board requirements as determined in consultation with the human subjects advisor for the National Center for Emerging and Zoonotic Infectious Disease.

All visits during 2010-2011 were included unless resulting in hospital or observation unit admission or if parenteral antibiotics were mentioned without oral antibiotics (0.4% of visits). National estimates were produced from 184 032 unweighted visits in 2010-2011. Antibiotics were coded in terms of their generic components and therapeutic classes using Lexicon Plus (Cerner Multum).[16] Data were not available on route of administration. Antibiotics supplied only in topical formulations were excluded. Oral antibiotics were defined as antibiotics with oral formulations, and parenteral antibiotics were defined as those antibiotics not available in oral formulations (eTable 1 in the Supplement). As outpatient, oral antibiotics are only available via prescription, medication mentions of antibiotics were assumed to be prescriptions, similar to previous studies.[17-19]

Establishing the Baseline

The mean annual rates per 1000 population of visits with antibiotic prescriptions by age group (0-2, 3-9, 10-19, 20-39, 40-64, ≥65 years) and US Census region (Northeast, South, Midwest, and West) for 2010-2011 were calculated. The Northeast region included Maine, New Hampshire, Vermont, Massachusetts, Rhode Island, Connecticut, New York, New Jersey, and Pennsylvania. The Midwest region included Ohio, Michigan, Indiana, Illinois, Wisconsin, Missouri, Iowa, Minnesota, Kansas, Nebraska, South Dakota, and North Dakota. The South region included Delaware, Maryland, District of Columbia, Virginia, West Virginia, North Carolina, South Carolina, Florida, Georgia, Tennessee, Kentucky, Alabama, Mississippi, Louisiana, Arkansas, Oklahoma, and Texas. The West region included Montana, Wyoming, Colorado, New Mexico, Arizona, Utah, Idaho, Washington, Oregon, Nevada, California, Alaska, and Hawaii. The mean annual rate per 1000 population, number,

Copyright 2016 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ by Arnab Mukherjee on 03/09/2020

and percentage of visits with antibiotics prescribed were also calculated by diagnosis and age group. For diagnosis-based analyses, larger age groups (0-19, 20-64, ≥65 years) were used to produce more reliable estimates.

Diagnostic categories for common outpatient infections (eTable 2 in the Supplement) were established and visits were classified into these categories. As NAMCS/NHAMCS do not contain links between diagnoses and medication mentions, visit diagnoses were classified based on the most likely indication for an antibiotic prescription in a tiered fashion. Tier 1 diagnoses were diagnoses for which antibiotics are almost always indicated: pneumonia, urinary tract infection (UTI), or miscellaneous bacterial infections (eg, pertussis and syphilis). Tier 2 diagnoses are diagnoses for which antibiotics may be indicated: sinusitis; suppurative otitis media; skin, cutaneous, and mucosal infections; pharyngitis; gastrointestinal infections; and acne. Tier 3 diagnoses were all other diagnostic categories for which antibiotics are not indicated or the indication was unclear. In assigning each visit a single diagnosis, priority was given to tier 1 diagnoses, then tier 2 diagnoses, then tier 3 diagnoses. If a visit had multiple diagnoses from a single tier, the first-listed diagnosis was assigned.

Estimating Appropriate Antibiotic Prescribing

To estimate appropriate oral antibiotic prescribing in ambulatory care, the Pew Charitable Trusts convened a group of experts on outpatient antibiotic use to determine methods for estimating the fraction of antibiotic use that is appropriate. Each author reviewed available national guidelines from professional societies for common conditions (eTable 3 in the Supplement). Estimated levels of appropriate antibiotic prescribing by age group were based on national guidelines for diagnoses for which national guidelines could be used to recommend specific antibiotic prescribing rates: pharyngitis; asthma, allergy; bronchitis, bronchiolitis; influenza; nonsuppurative otitis media; viral upper respiratory tract infection; viral and nonviral pneumonia; UTI; and miscellaneous bacterial infections (eg, pertussis and syphilis). Regional variability was used to produce estimates of appropriate antibiotic prescriptions for diagnoses for which guidelines could not be used to recommend specific antibiotic prescribing rates: sinusitis, suppurative otitis media, and the remaining other conditions. Regional analyses of antibiotic prescribing by age group were conducted to identify regions with the lowest regional antibiotic prescription rates, recognizing there is evidence of antibiotic overuse even in the lowest-prescribing regions.[20] Estimates were combined using national guidelines and regional variability to calculate an overall estimate of appropriate antibiotic prescriptions per 1000 population.

Statistical Analysis

Statistical analyses were performed using STATA 12 (STATA Corp) and accounted for the components of the complex survey design including patient visit weights, strata, and primary sampling unit design variables. Two years of survey data were combined for analyses to increase sample size by age and diagnosis. Ninety-five percent confidence intervals were calculated for all estimates. Antibiotic prescribing rates were compared using χ^2 test for heterogeneity. Estimates were not calculated if based on fewer than 30 sampled visits or if the relative standard error was less than 0.3, as such estimates do not meet standards of reliability or precision.[16] Significance was considered at 2-sided *P* value less than .05. Population denominators were based on the July 1, 2010, and July 1, 2011, set of estimates of the civilian, noninstitutional population of the United States, as developed by the Population Division, US Census Bureau.[21] Additionally, a post hoc sensitivity analysis was performed using the lowest-prescribing region as the benchmark for all estimates of appropriate antibiotic prescribing for diagnoses targeted for reduction.

Results

In 2010-2011, of the 184 032 sampled ambulatory care visits, 12.6% (95% CI, 12.0%-13.3%) were associated with antibiotic prescriptions (**Table 1**), with an estimated 506 antibiotic prescriptions (95% CI, 458-554) per 1000 US population annually (**Table 2**). Per 1000 population, antibiotic prescribing rates ranged from 423 antibiotic prescriptions (95% CI, 343-504) in the West to 553 antibiotic prescriptions (95% CI, 459-648) in the South (**Table 3**). The annual antibiotic prescription rate was highest among children aged 0 through 2 years at 1287 antibiotic prescriptions (95% CI, 1085-1489) per 1000 population.

The top 3 diagnoses associated with antibiotic prescriptions per 1000 population were sinusitis (56 antibiotic prescriptions [95% CI, 48-64]), suppurative otitis media (47 antibiotic prescriptions [95% CI, 41-54]), and pharyngitis (43 antibiotic prescriptions [95% CI, 38-49]) (Table 2). Collectively, acute respiratory conditions, defined as sinusitis, suppurative otitis media, nonsuppurative otitis media, pharyngitis, viral upper respiratory tract infection, bronchitis and bronchiolitis, asthma and allergy, influenza and viral and nonviral pneumonia, were associated with an estimated 221 antibiotic prescriptions (95% CI, 198-245) per 1000 population annually.

For pharyngitis, national guidelines recommend antibiotic therapy only for streptococcal pharyngitis.[7] Based on recent literature, 37% of children presenting for medical visits with sore throat tested positive for group A *Streptococcus*.[22,23] However, 56.2% of visits (95% CI, 49.8%-62.4%) by children with pharyngitis were associated with antibiotic prescribing in 2010-2011 (Table 1). For adults presenting for medical visits with sore throat, about 18% have streptococcal pharyngitis (ie, meet clinical criteria and have a positive test result for group A *Streptococcus*),[7,23] but 72.4% (95% CI, 66.8%-77.4%) of visits by adults aged 20 through 64 years with pharyngitis were associated with antibiotic prescribing.

National guidelines state that patients with bronchitis (excluding visits with diagnoses of chronic bronchitis, emphysema, or chronic obstructive pulmonary disease),[24,25] bronchiolitis,[26] viral upper respiratory tract infections,[25,27] asthma and allergy,[28] influenza,[29] viral pneumonia[30] and nonsuppurative otitis media[31] should not receive antibiotics, and thus antibiotics for these conditions were considered inappropriate.

Copyright 2016 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ by Arnab Mukherjee on 03/09/2020

Table 1. Sampled Visits and Ambulatory Care Visits With Antibiotics Prescribed by Age Group and Diagnosis From the US NAMCS/NHAMCS, 2010-2011

	Age Group, y							
	0-19		20-64		≥65		All Ages	
Diagnosis[a]	Unweighted No. Sampled Visits	Weighted Visits With Antibiotics Prescribed, % (95% CI)	Unweighted No. Sampled Visits	Weighted Visits With Antibiotics Prescribed, % (95% CI)	Unweighted No. Sampled Visits	Weighted Visits With Antibiotics Prescribed, % (95% CI)	Unweighted No. Sampled Visits	Weighted Visits With Antibiotics Prescribed, % (95% CI)
Sinusitis	549	84.7 (79.1-89.0)	1492	70.9 (66.4-75.0)	256	53.8 (44.4-62.9)	2297	72.2 (68.2-75.9)
Suppurative otitis media	2083	82.0 (78.2-85.3)	415	69.0 (59.1-77.4)	50	[b]	2548	79.5 (76.0-82.7)
Pharyngitis	1580	56.2 (49.8-62.4)	1107	72.4 (66.8-77.4)	65	[b]	2752	62.2 (57.2-67.0)
Skin, cutaneous, and mucosal infections	1053	48.7 (42.8-54.7)	2591	53.5 (50.0-57.0)	536	39.8 (31.6-48.5)	4180	50.0 (46.9-53.1)
Other skin, cutaneous, and mucosal conditions	4631	11.3 (9.4-13.4)	8828	11.0 (9.1-13.2)	4654	6.5 (4.4-9.5)	18 113	9.6 (8.0-11.5)
Urinary tract infections	554	73.2 (63.9-80.9)	1821	75.0 (69.4-80.0)	627	65.2 (56.8-72.8)	3002	72.2 (67.7-76.3)
Viral upper respiratory tract infection	2083	21.2 (16.9-26.3)	931	43.0 (36.7-49.5)	200	39.4 (27.2-53.1)	3214	29.6 (25.7-33.8)
Bronchitis or bronchiolitis[c]	491	55.2 (45.3-64.8)	821	72.4 (60.1-82.1)	193	60.9 (45.9-74.0)	1505	64.5 (56.6-71.6)
Other gastrointestinal conditions	1338	9.3 (6.3-13.3)	4252	14.8 (12.4-17.5)	1007	8.3 (5.6-12.2)	6597	12.4 (10.7-14.4)
Other genitourinary conditions	702	16.1 (12.0-21.4)	4739	10.7 (8.8-12.9)	1315	10.6 (8.2-13.6)	6756	11.1 (9.6-12.8)
Miscellaneous bacterial infections	1693	14.0 (10.4-18.5)	1895	19.5 (15.9-23.7)	215	29.0 (17.8-43.4)	3803	17.7 (15.0-20.7)
Other respiratory conditions (eg, chronic bronchitis)	510	23.5 (15.6-33.7)	1234	15.7 (11.9-20.4)	854	15.2 (11.4-20.0)	2598	16.8 (14.0-20.2)
Gastrointestinal infections	1729	10.4 (7.2-14.6)	4409	10.1 (8.0-12.6)	862	8.0 (4.9-12.7)	7000	9.7 (8.0-11.8)
Pneumonia	348	79.2 (69.1-86.6)	295	56.5 (47.0-65.7)	183	36.6 (24.7-50.5)	826	61.3 (54.1-68.0)
Acne	321	46.4 (38.9-54.1)	273	41.5 (33.6-49.9)	11	[b]	605	43.8 (38.2-49.5)
Asthma or allergy	1572	9.2 (7.3-11.4)	1398	12.0 (9.0-15.8)	236	7.5 (3.8-14.3)	3206	10.3 (8.4-12.4)
Miscellaneous nonbacterial infections	299	[c]	752	10.8 (7.1-16.1)	112	[b]	1163	8.4 (5.7-12.3)
Nonsuppurative otitis media	269	22.2 (16.0-30.0)	93	[b]	26	[b]	388	20.3 (14.9-27.0)
Influenza	76	[b]	113	[b]	9	[b]	198	[b]
Viral pneumonia	5	[b]	4	[b]	0	[b]	9	[b]
Remaining codes not listed elsewhere	20 944	3.2 (2.7-3.7)	69 564	3.6 (3.2-3.9)	22 764	4.2 (3.7-4.7)	113 272	3.7 (3.4-4.0)
All conditions	42 830	19.5 (18.1-20.9)	107 027	11.7 (10.9-12.5)	34 175	8.4 (7.7-9.2)	184 032	12.6 (12.0-13.3)

Abbreviation: NAMCS/NHAMCS, National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey.

[a] Diagnostic categories were created based on the most likely indication for an antibiotic prescription in a tiered fashion. Tier 1 diagnoses were those in which antibiotics are almost always indicated: pneumonia, urinary tract infection, or miscellaneous bacterial infections (eg, pertussis and syphilis). Tier 2 diagnoses are those for which antibiotics may be indicated: sinusitis, suppurative otitis media; skin, cutaneous, and mucosal infections, pharyngitis, gastrointestinal infections, and acne. Tier 3 diagnoses were all other diagnostic categories for which antibiotics are not indicated. In assigning each visit a single diagnosis, priority was given to tier 1 diagnoses, then tier 2 diagnoses, then tier 3 diagnoses. See eTable 2 in the Supplement for full details and included *International Classification of Diseases, Ninth Revision, Clinical Modification* codes for diagnostic categories.

[b] Value does not meet standard of reliability or precision.

[c] Bronchitis or bronchiolitis includes visits with bronchitis, not specified as acute or chronic, and acute bronchitis and bronchiolitis but excludes visits in which the second or third diagnosis was chronic bronchitis, emphysema, or chronic obstructive pulmonary disease.

Sinusitis and suppurative otitis media sometimes warrant antibiotics; however, the appropriate rate of antibiotic prescriptions for these conditions is uncertain. Thus, the lowest regional rate of visits with antibiotic prescriptions was selected as the estimate of the appropriate rate (eTable 4 in the Supplement). For sinusitis, the estimated appropriate antibiotic prescription rates per 1000 participants by age group were as follows: 59 (95% CI, 32-86) for 0 through 19 years, 27 (95% CI, 17-36) for 20 through 64 years, and 37 (95% CI, 16-59) for 65 years and older. For suppurative otitis media, the estimated appropriate antibiotic prescription rates per 1000 participants by age group were as follows: 138 (95% CI, 96-179) for 0 through 19 years and 6 (95% CI, 4-9) for 20 through 64 years. Estimates could not be calculated for adults aged 65 years

Copyright 2016 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ by Arnab Mukherjee on 03/09/2020

Table 2. Sampled Visits With Antibiotics Prescribed and Mean Annual Rate per 1000 Population of Ambulatory Care Visits With Antibiotics Prescribed by Age Group and Diagnosis From the US NAMCS/NHAMCS, 2010-2011

Diagnosis[a]	Age Group, y							
	0-19		20-64		≥65		All Ages	
	Unweighted No. of Sampled Visits With Antibiotics Prescribed	Weighted Mean Annual Rate of Visits With Antibiotics Prescribed, % (95% CI)[b,c]	Unweighted No. of Sampled Visits With Antibiotics Prescribed	Weighted Mean Annual Rate of Visits With Antibiotics Prescribed, % (95% CI)[b,c]	Unweighted No. of Sampled Visits With Antibiotics Prescribed	Weighted Mean Annual Rate of Visits With Antibiotics Prescribed, % (95% CI)[b,c]	Unweighted No. Sampled Visits With Antibiotics Prescribed	Weighted Mean Annual Rate of Visits With Antibiotics Prescribed, % (95% CI)[b,c]
Sinusitis	457	65 (51-79)	1055	55 (45-64)	151	44 (32-57)	1663	56 (48-64)
Suppurative otitis media	1660	154 (131-177)	305	9 (7-11)	23	[d]	1988	47 (41-54)
Pharyngitis	1001	91 (76-105)	785	29 (23-35)	39	[d]	1825	43 (38-49)
Skin, cutaneous, and mucosal infections	570	39 (32-46)	1493	39 (33-44)	230	38 (29-47)	2293	39 (34-43)
Other skin, cutaneous, and mucosal conditions	607	37 (30-43)	1321	32 (25-39)	384	64 (39-89)	2312	38 (30-45)
Urinary tract infections	436	23 (17-28)	1465	35 (30-41)	459	64 (51-77)	2360	35 (31-40)
Viral upper respiratory tract infections	369	42 (31-53)	371	19 (15-23)	79	29 (16-41)	819	26 (21-31)
Bronchitis or bronchiolitis[e]	259	28 (18-39)	608	23 (18-28)	140	30 (20-40)	1007	25 (20-30)
Other gastrointestinal conditions	132	9 (5-12)	947	21 (17-25)	85	19 (10-28)	1164	17 (14-21)
Other genitourinary conditions	133	8 (5-11)	646	19 (14-23)	144	31 (22-40)	923	17 (14-21)
Miscellaneous bacterial infections	272	20 (13-26)	390	11 (9-13)	40	[d]	702	14 (11-17)
Other respiratory conditions (eg, chronic bronchitis)	73	10 (6-14)	210	7 (5-9)	117	33 (21-45)	400	11 (8-14)
Gastrointestinal infections	112	10 (6-13)	423	11 (9-14)	65	13 (7-20)	600	11 (9-13)
Pneumonia	275	22 (16-27)	219	5 (4-7)	105	12 (7-17)	599	11 (9-13)
Acne	134	22 (17-27)	119	8 (5-11)	3	[d]	256	11 (8-13)
Asthma or allergy	125	14 (9-18)	189	8 (6-11)	30	[d]	344	9 (7-12)
Miscellaneous nonbacterial infections	23	[d]	105	3 (1-4)	7	[d]	135	2 (1-3)
Nonsuppurative otitis media	81	5 (3-7)	21	[d]	3	[d]	105	2 (1-3)
Influenza	5	[d]	14	[d]	1	[d]	20	[d]
Viral pneumonia	2	[d]	1	[d]	0	[d]	3	[d]
Remaining codes not listed elsewhere	784	48 (39-57)	2479	83 (71-95)	936	200 (166-234)	4199	89 (77-100)
All conditions	7510	646 (571-721)	13 166	418 (372-464)	3041	617 (544-689)	23 717	506 (458-554)

Abbreviation: NAMCS/NHAMCS, National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey.

[a] Diagnostic categories were created based on the most likely indication for an antibiotic prescription in a tiered fashion. Tier 1 diagnoses were those in which antibiotics are almost always indicated: pneumonia, urinary tract infection, or miscellaneous bacterial infections (eg, pertussis and syphilis). Tier 2 diagnoses are those for which antibiotics may be indicated: sinusitis, suppurative otitis media; skin, cutaneous, and mucosal infections, pharyngitis, gastrointestinal infections, and acne. Tier 3 diagnoses were all other diagnostic categories for which antibiotics are not indicated. In assigning each visit a single diagnosis, priority was given to tier 1 diagnoses, then tier 2 diagnoses, then tier 3 diagnoses. See eTable 2 in the Supplement for full details and included *International Classification of Diseases, Ninth Revision, Clinical Modification* codes for diagnostic categories.

[b] Values are based on 2-year averages.

[c] Population denominators are based on the July 1, 2010, and July 1, 2011, set of estimates of the civilian, noninstitutional population of the United States, as developed by the Population Division of the US Census Bureau.[21]

[d] Figure does not meet standard of reliability or precision.

[e] Bronchitis or bronchiolitis includes visits with bronchitis, not specified as acute or chronic, and acute bronchitis and bronchiolitis but excludes visits in which the second or third diagnosis was chronic bronchitis, emphysema, or chronic obstructive pulmonary disease.

or older with suppurative otitis media due to the small number of sampled visits.

Antibiotic prescription rates were considered appropriate for pneumonia because the diagnosis almost always warrants antibiotic therapy.[30]

For other conditions, excluding acute respiratory conditions listed above, antibiotic prescriptions were considered appropriate for UTI and miscellaneous bacterial infections (eg, pertussis and syphilis), as these conditions almost always warrant antibiotic therapy.[32] For the remaining other conditions (excluding acute respiratory conditions, UTIs, and miscellaneous bacterial infections), the lowest regional rate of visits with antibiotic prescriptions per 1000 participants by age group was selected as the estimated appropriate rate (eTable 4 in the Supplement): 137 (95% CI, 100-174) for 0 through 19 years, 180 (95% CI, 140-220) for 20 through 64 years, and 362 (95% CI, 272-452) for 65 years or older.

Copyright 2016 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ by Arnab Mukherjee on 03/09/2020

Table 3. Mean Annual Total Visit Rate and Rate of Visits With Antibiotics Prescribed per 1000 Population by US Census Region and Age Group From the US NAMCS/NHAMCS, 2010-2011[a]

	Ambulatory Visits, Weighted Mean Annual Rate per 1000 Population (95% CI)										P Value for Weighted Rate	
	Northeast[b]		Midwest[c]		South[d]		West[e]		Total			
Age Group, y	Total	Antibiotics Prescribed	Total	Antibiotics Prescribed	Total	Antibiotics Prescribed	Total	Antibiotics Prescribed	Total	Antibiotics Prescribed	Total Among Regions[f]	Antibiotic Prescriptions Among Regions[g]
0-2	8203 (6078-10 329)	1196 (703-1689)	6021 (4862-7181)	1240 (877-1602)	6837 (5292-8381)	1492 (1098-1885)	6717 (5514-7919)	1071 (752-1390)	6851 (6070-7633)	1287 (1085-1489)	.35	.45
3-9	4178 (3325-5031)	864 (562-1167)	2326 (1925-2726)	535 (398-673)	2862 (2156-3568)	738 (576-899)	2836 (2338-3335)	597 (459-735)	2953 (2617-3289)	680 (590-771)	.002	.11
10-19	3149 (2547-3750)	510 (342-769)	2441 (2015-2866)	406 (331-480)	2654 (2149-3159)	491 (395-587)	2110 (1669-2550)	345 (255-436)	2563 (2307-2819)	441 (388-494)	.05	.11
20-39	3410 (3021-3799)	393 (311-475)	2968 (2329-3606)	418 (314-523)	3024 (2509-3538)	469 (362-576)	2542 (2030-3055)	272 (196-347)	2962 (2689-3235)	397 (346-448)	.07	.01
40-64	4556 (4015-5098)	440 (336-545)	3913 (3161-4664)	463 (351-574)	4031 (3313-4748)	463 (376-551)	3942 (3374-4510)	359 (281-437)	4083 (3732-4434)	435 (387-483)	.37	.27
≥65	7536 (6330-8743)	623 (434-813)	6854 (5610-8097)	592 (453-732)	7056 (5791-8322)	594 (477-711)	8046 (6901-9190)	675 (521-830)	7317 (6676-7959)	617 (544-689)	.51	.85
All ages	4580 (4047-5114)	525 (431-618)	3786 (3155-4418)	497 (398-596)	3970 (3311-4629)	553 (459-648)	3796 (3262-4330)	423 (343-504)	3999 (3678-4320)	506 (458-554)	.15	.18

Abbreviation: NAMCS/NHAMCS, National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey.

[a] Population denominators are based on the July 1, 2010, and July 1, 2011, set of estimates of the civilian, noninstitutional population of the United States, as developed by the Population Division of the US Census Bureau.[21,22] Values are based on 2-year averages.

[b] Northeast region includes Maine, New Hampshire, Vermont, Massachusetts, Rhode Island, Connecticut, New York, New Jersey, and Pennsylvania.

[c] Midwest region includes Ohio, Michigan, Indiana, Illinois, Wisconsin, Missouri, Iowa, Minnesota, Kansas, Nebraska, South Dakota, and North Dakota.

[d] South region includes Delaware, Maryland, District of Columbia, Virginia, West Virginia, North Carolina, South Carolina, Florida, Georgia, Tennessee, Kentucky, Alabama, Mississippi, Louisiana, Arkansas, Oklahoma, and Texas.

[e] West region includes Montana, Wyoming, Colorado, New Mexico, Arizona, Utah, Idaho, Washington, Oregon, Nevada, California, Alaska, and Hawaii.

[f] *P* values are for χ^2 test for heterogeneity for differences among regions for rate of total visits per 1000 population.

[g] *P* values are for χ^2 test for heterogeneity for differences among regions for rate of antibiotics prescriptions per 1000 population.

The actual and estimated appropriate antibiotic prescription rates by age group for each condition and overall are shown in **Table 4**. The estimated annual appropriate antibiotic prescription rate for acute respiratory conditions per 1000 population was 111 antibiotic prescriptions for all ages vs 221 antibiotic prescriptions (95% CI, 198-245) annually for acute respiratory conditions in 2010-2011, a 50% reduction from the point estimate of the 2010-2011 annual rate. The estimated annual appropriate rate per 1000 population for other conditions (excluding acute respiratory) was 242 antibiotic prescriptions vs 284 (95% CI, 256-313) annually in 2010-2011, a 15% reduction from the point estimate of the 2010-2011 annual rate. When all conditions were combined, the estimated appropriate annual antibiotic prescription rate for all conditions in all ages in the United States per 1000 population was 353 vs 506 (95% CI, 458-554) annually in 2010-2011, a 30% reduction from the point estimate of the 2010-2011 annual rate. The results of the sensitivity analysis using the lowest-prescribing region as the estimate of appropriate antibiotic prescribing for all diagnoses identified for reduction are shown in eTable 5 in the Supplement.

Discussion

These analyses describe antibiotic prescribing practices during ambulatory care visits in the United States by age group and diagnosis in 2010-2011, with an overall estimated annual rate of 506 antibiotic prescriptions per 1000 US population. In the United States, an estimated 154 million prescriptions for antibiotics were written in ambulatory care settings annually during 2010-2011. Half of antibiotic prescriptions for acute respiratory conditions may have been unnecessary, representing 34 million antibiotic prescriptions annually. Collectively, across all conditions, an estimated 30% of outpatient, oral antibiotic prescriptions may have been inappropriate. Therefore, a 15% reduction in overall antibiotic use would be necessary to meet the White House National Action Plan for Combating Antibiotic-Resistant Bacteria goal of reducing inappropriate antibiotic use in the outpatient setting by 50% by 2020.[12] This estimate of inappropriate outpatient antibiotic prescriptions can be used to inform antibiotic stewardship programs in ambulatory care by public health and health care delivery systems in the next 5 years.

This estimate of inappropriate outpatient antibiotic prescriptions is based on deriving an estimate for the rate of ambulatory care visits during which antibiotics are prescribed when not

Copyright 2016 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ by Arnab Mukherjee on 03/09/2020

Table 4. Mean Annual Antibiotic Prescribing Rates in 2010-2011 US NAMCS/NHAMCS vs Estimated Appropriate Antibiotic Prescribing Annual Rates per 1000 Population by Age Group and Diagnosis

	Rates per 1000 Population		Potential Reduction in Annual Antibiotic Prescription Rates, %
	2010-2011 Weighted Mean Annual Rate of Antibiotic Prescriptions (95% CI)	Estimated Appropriate Annual Rate of Antibiotic Prescriptions[a]	
0-19 y			
All acute respiratory conditions[b]	421 (369 to 473)	278[c]	−34
Sinusitis	65 (51 to 79)	59	−9
Suppurative otitis media	154 (131 to 177)	138	−10
Pharyngitis	91 (76 to 105)	60	−34
Asthma or allergy; bronchitis or bronchiolitis; influenza; nonsuppurative otitis media; viral URI; and viral pneumonia[e]	90 (71 to 108)	0	−100
Pneumonia	22 (16 to 27)	22	0
Other conditions[d]	225 (197 to 252)	180[f]	−20
Urinary tract infection	23 (17 to 28)	23	0
Miscellaneous bacterial infections	20 (13 to 26)	20	0
Remaining other conditions[g]	182 (160 to 205)	137	−25
Total[h]	646 (571 to 721)	458	−29
20-64 y			
All acute respiratory conditions[b]	150 (129 to 170)	45[c]	−70
Sinusitis	55 (45 to 64)	27	−51
Suppurative otitis media	9 (7 to 11)	6	−33
Pharyngitis	29 (23 to 35)	7	−75
Asthma or allergy; bronchitis or bronchiolitis; influenza; nonsuppurative otitis media; viral URI; and viral pneumonia[e]	52 (43 to 60)	0	−100
Pneumonia	5 (4 to 7)	5	0
Other conditions[d]	269 (239 to 298)	227[f]	−16
Urinary tract infection	35 (30 to 41)	35	0
Miscellaneous bacterial infections	11 (9 to 13)	11	0
Remaining other conditions[g]	222 (197 to 248)	180	−19
Total[h]	418 (372 to 464)	272	−35
≥65 y			
All acute respiratory conditions[b]	136 (111 to 162)	63[c]	−54
Sinusitis	44 (32 to 57)	37	−16
Asthma or allergy; bronchitis or bronchiolitis; influenza; nonsuppurative otitis media; viral URI; and viral pneumonia[e]	66 (48 to 84)	0	−100
Pneumonia	12 (7 to 17)	12	0
Other conditions[d]	480 (418 to 543)	441[f]	−8
Urinary tract infection	64 (51 to 77)	64	0
Remaining other conditions[g]	401 (346 to 456)	362	−10
Total[h]	617 (544 to 689)	504	−18
All Ages			
All acute respiratory conditions[b]	221 (198 to 245)	111	−50
Other conditions[d]	284 (256 to 313)	242	−15
Total[h]	506 (458 to 554)	353	−30

Abbreviations: NAMCS/NHAMCS, National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey; URI, upper respiratory tract infection.

[a] Targets based on lowest-prescribing regions for sinusitis, suppurative otitis media, and remaining other conditions; percent streptococcal pharyngitis for pharyngitis (37% for children, 18% adults); no antibiotics for asthma, allergy; bronchitis, bronchiolitis; influenza; nonsuppurative otitis media; URI; and viral pneumonia; no change in antibiotic prescribing for pneumonia, urinary tract infection, and miscellaneous bacterial infections. See Results section for further details.

[b] All acute respiratory conditions include suppurative and nonsuppurative otitis media; sinusitis; pharyngitis; pneumonia; bronchitis, bronchiolitis; URI; influenza, asthma, allergy, and viral pneumonia.

[c] Difference between the 2010-2011 antibiotic rate for all acute respiratory conditions and sum of the differences between the current and estimated appropriate antibiotic rate for each acute respiratory condition.

[d] Other conditions excluding acute respiratory conditions listed above.

[e] Bronchitis or bronchiolitis includes visits with bronchitis, not specified as acute or chronic, and acute bronchitis and bronchiolitis but excludes visits in which the second or third diagnosis was chronic bronchitis, emphysema, or chronic obstructive pulmonary disease.

[f] Difference between the current antibiotic rate for other conditions and sum of the differences between the 2010-2011 and estimated appropriate antibiotic rate for urinary tract infection, miscellaneous bacterial infections, and remaining other conditions.

[g] Remaining other conditions exclude acute respiratory conditions, urinary tract infection, and miscellaneous bacterial infections.

[h] Sum of acute respiratory conditions and other conditions, slight differences may be present in sums due to rounding.

indicated and for diagnoses that are overused (eg, sinusitis). To derive this estimate, a conservative, mixed approach was used including (1) no reductions for conditions almost always warranting antibiotics, (2) application of clinical guidelines for nonbacterial respiratory conditions, (3) an estimate for group A streptococcal prevalence for pharyngitis, based on evidence-based guidelines, and (4) use of geographic variability by focusing on regions with the lowest antibiotic prescribing rates for suppurative otitis media, sinusitis, and remaining conditions. Previous studies estimating potential estimates of inappropriate outpatient antibiotic use have relied solely on estimates of bacterial prevalence and have concluded that more than 50% of antibiotics for acute respiratory tract infections are unnecessary.[17,18] Although knowledge of bacterial pathogen presence could be informative, routine performance of sinus aspiration or tympanocentesis is impractical. Current treat-

Copyright 2016 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ by Arnab Mukherjee on 03/09/2020

ment guidelines for sinusitis and otitis media advocate using stringent clinical criteria for diagnosis and to identify candidates for watchful waiting and antibiotic therapy,[8-10,33] but the fraction of diagnoses that meet these criteria is unknown.

A substantial amount of antibiotic overuse is likely driven by overdiagnosis of certain conditions (eg, sinusitis diagnosis without meeting criteria). Evidence supporting the problem of overdiagnosis, in particular for sinusitis and otitis media, includes variability in diagnosis by race and by clinician.[34] Although the health of the populations in each region and thus the need for antibiotic use may vary, the regional analyses from which the estimated appropriate rates are taken are based on large regions with populations ranging from 55 million (Northeast) to 113 million (South). To our knowledge, no data suggest worse outcomes for these conditions in low-prescribing regions due to undertreatment; in fact, there is evidence of antibiotic overuse even in low-prescribing regions.[20] For pneumonia, UTI and miscellaneous bacterial infections, no specific goal was recommended at this time, even though overdiagnosis of these conditions likely occurs, particularly with asymptomatic bacteriuria diagnosed as UTI. For this effort, the group focused on conditions for which the diagnoses often or sometimes do not require antibiotics, rather than misdiagnosis of conditions almost always requiring antibiotics. Misdiagnosis will present important opportunities in the future, especially for infections like UTI and community-acquired pneumonia.

The geographic variation nationally and globally indicates that a 30% reduction in antibiotic prescribing is achievable. Per the sensitivity analysis, if national antibiotic prescriptions rates for targeted diagnoses for each age group were at the rate of the lowest-prescribing region, prescribing would be 19% lower than the 2010-2011 rate. However, when low-prescribing regions are used to produce estimates for appropriate prescribing, more antibiotic prescriptions are considered appropriate than when estimates are based on national guidelines.

Another study examining dispensed antibiotics found the lowest-prescribing 5 states dispensed 36% fewer antibiotic prescriptions than the United States overall; this study found a similar pattern to our study of higher prescribing in the South vs the West.[4] Sweden dispensed 328 antibiotic courses per 1000 population in 2014[3] compared with 877 antibiotic courses dispensed per 1000 population in the United States in 2011.[35] Sweden has very low rates antibiotic-resistant infections.[36] By reducing antibiotic prescribing for common infections, 1 potential concern is increasing suppurative complications. However, in Sweden, acute otitis media diagnoses and antibiotic use decreased during 2000-2005 by 50%, likely due to stricter diagnostic criteria and educational campaigns, with no increase in mastoiditis,[37] all prior to introduction of pneumococcal conjugate vaccine.[38] Effective interventions to reduce inappropriate prescribing, such as clinician and patient education, audit-and-feedback, academic detailing, communication training, rapid diagnostics, clinical decision support, and delayed prescriptions, can be used in ambulatory care settings to improve appropriate antibiotic use.[39]

Strengths of NAMCS/NHAMCS include national representativeness and inclusion of both diagnoses and therapy. However, the use of NAMCS/NHAMCS in this study also has the following limitations. First, the NAMCS and NHAMCS rely on clinician diagnoses and lack data allowing for validation of diagnoses and links between medications and diagnoses. *ICD-9-CM* codes, although assigned by NAMCS/NHAMCS staff, lack specificity to differentiate all diagnoses of interest and may not fully represent the clinician's diagnosis. NAMCS/NHAMCS allow for 3 diagnoses, and if the visit lacked antibiotic-appropriate diagnosis, it was assumed that none existed. However, all 3 diagnoses fields were used and antibiotic prescribing was considered appropriate if there was any antibiotic-appropriate diagnosis.

Second, estimates in NAMCS and NHAMCS are adjusted for nonresponse for a limited number of variables, and thus nonresponse bias may be present.[40]

Third, data from NAMCS and NHAMCS represent visits, not illness episodes, such that multiple prescriptions for 1 person would be captured separately, and therefore the overall estimated rates of antibiotic prescribing per population and inappropriate prescribing may be overestimated. For instance, in 2010-2011 in NAMCS/NHAMCS, an estimated 1.2 billion ambulatory care visits occurred annually from a population of 305 million people in the United States, suggesting that, on average, approximately 4 ambulatory care visits occurred for each person in the United States. In reality, some individuals had more than 4 ambulatory care visits, and some had fewer or no visits. Of these projected 1.2 billion visits annually, an estimated 12.6% were associated with antibiotic prescriptions, which would equate to a projected 154 million antibiotic prescriptions written annually in these settings or an estimated population-based rate of 506 antibiotic prescriptions per 1000 US population (ie, every person in the population would have received 0.5 antibiotic prescriptions per year from an office or emergency department-based visit). However, some patients received no antibiotic prescriptions, and some likely received more than 1 antibiotic prescription. In addition, because some individuals had multiple visits and would have been sampled multiple times, it is almost certain that complex patients (who would have many visits annually) are overrepresented in the study population compared with truly "typical" patients, and far more than healthy patients, who may not have had any visits during the sampling frame. It also is possible that for these complex patients, what may seem like inappropriate prescriptions could have been appropriate. Moreover, the more times an individual sees a physician, the more likely that patient will get a prescription, independent of whether the prescription was appropriate or not. However, these multiple exposures for an individual are treated as "on average" a single exposure for multiple individuals and the data were not adjusted for comorbidities or for the number of times an individual is included in the sampling frame, suggesting that the overall estimated rate of antibiotic prescribing per population may be biased upward.

Fourth, NAMCS/NHAMCS also have significant time delays, limiting the ability to use data more recent than 2011. The

Copyright 2016 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ by Arnab Mukherjee on 03/09/2020

same analysis of 2008-2009 data showed that antibiotic prescribing patterns were stable from 2008-2011 and that 31% of 2008-2009 outpatient antibiotic prescriptions were unnecessary. More recent data indicate that overall outpatient antibiotic courses dispensed have remained stable from 2011 through 2013 with 877 and 849 antibiotic courses dispensed per 1000 population, respectively.[35] The rate of antibiotic prescriptions in this study is just more than half the rate of antibiotics dispensed in outpatient settings in the United States in 2011.[4,35] It is not known how these rates in this study based on data from 2010-2011 compare or reflect the rates of prescribing in 2016.

Fifth, antibiotics prescribed at urgent care and retail clinic, federal facilities, hospital discharges, telemedicine encounters and for long-term care residents are not included in NAMCS/NHAMCS. In addition, visits to physician assistants and nurse practitioners are not systematically sampled and may be underrepresented.

Sixth, these data reflect medication mentions, not antibiotics dispensed or consumed, and delayed prescriptions cannot be differentiated from standard prescriptions. Appropriate antibiotic selection was not addressed, but a separate study is under way to identify opportunities to improve selection.

Conclusions

In the United States in 2010-2011, there was an estimated annual antibiotic prescription rate per 1000 population of 506, but only an estimated 353 antibiotic prescriptions were likely appropriate, supporting the need for and establishing a goal for outpatient antibiotic stewardship.

ARTICLE INFORMATION

Author Affiliations: Centers for Disease Control and Prevention, Atlanta, Georgia (Fleming-Dutra, Bartoces, Roberts, Sanchez, Hicks); Pediatric Infectious Diseases, University of Utah, Salt Lake City (Hersh); School of Medicine, University of California, San Francisco, San Francisco (Shapiro); Division of Health Policy and Management, University of Minnesota, Minneapolis (Enns); Summa Health System and Northeast Ohio Medical University, Akron (File); Boston Children's Hospital and Harvard Medical School, Boston, Massachusetts (Finkelstein); Children's Hospital of Philadelphia, Philadelphia, Pennsylvania (Gerber); University of Pennsylvania Perelman School of Medicine, Philadelphia (Gerber, Margolis); Pew Charitable Trusts, Washington, DC (Hyun, Zetts); Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts (Linder); Minnesota Department of Health, St Paul (Lynfield); Department of Emergency Medicine, University of California-Davis, Sacramento (May); Department of Family Medicine, Georgetown University Medical Center, Washington, DC (Merenstein); Division of General Internal Medicine, Massachusetts General Hospital, Boston (Metlay); Division of Pediatric Infectious Diseases, Washington University School of Medicine, St Louis, Missouri (Newland); Department of Otolaryngology-Head and Neck Surgery, Washington University School of Medicine, St Louis, Missouri (Piccirillo); Department of Veterans Affairs, University of Illinois at Chicago, Chicago (Suda); Oregon Public Health Division, Portland (Thomas); Pacific Lutheran University, Tacoma, Washington (Woo).

Author Contributions: Drs Fleming-Dutra and Hicks had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Fleming-Dutra, Hersh, Hicks.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Fleming-Dutra.
Critical revision of the manuscript: Hersh, Shapiro, Bartoces, Enns, File , Finkelstein, Gerber, Hyun, Linder, Lynfield, Margolis, May, Merenstein, Metlay, Newland, Piccirillo, Roberts, Sanchez, Suda, Thomas, Woo, Zetts, Hicks.
Statistical analysis: Shapiro.
Obtained funding: Hyun, Zetts.
Administrative, technical, or material support: Fleming-Dutra, Hyun, Zetts, Hicks.
Study supervision: Fleming-Dutra, Hersh, Hicks.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr File reports receiving grant funding from Cempra and Pfizer and personal fees from Actavis, Melinta, Merck, MotifBio, Nabriva, and Tetraphase. Dr Lynfield reports being co-editor for a book published by Wiley-Blackwell on Infectious Disease Surveillance for which royalties are donated to the Minnesota Department of Health. Dr Merenstein reports giving expert advice to Proctor and Gamble, Bayer, and Nestle. Dr Newland reports receiving grant funding from Pfizer and personal fees from RPS Diagnostics. No other disclosures are reported.

Funding/Support: This project was made possible through a partnership with the Centers for Disease Control and Prevention (CDC) Foundation. Support for this project was provided by Pew Charitable Trusts.

Role of the Funder/Sponsor: The CDC participated in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication. Pew Charitable Trusts participated in the interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication. Pew Charitable Trusts sponsored in-person and telephone author meetings and supported some author travel to in-person meetings.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC or the Department of Veterans Affairs.

Additional Contributions: We thank Tia Carter, MS, Allan Coukell, BSc Pharm, and Elizabeth Jungman, JD, MPH (all from Pew Charitable Trusts), for their assistance in convening author meetings. We also thank Allan Coukell, BSc Pharm (Pew Charitable Trusts), for his review of the manuscript. The above named individuals did not receive any compensation for their role in the study.

REFERENCES

1. Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States, 2013. http://www.cdc.gov/drugresistance/threat-report-2013/. Accessed April 11, 2016.

2. Linder JA. Editorial commentary: antibiotics for treatment of acute respiratory tract infections: decreasing benefit, increasing risk, and the irrelevance of antimicrobial resistance. *Clin Infect Dis*. 2008;47(6):744-746.

3. Swedres-Svarm Reports. Swedres-Svarm 2014. http://www.sva.se/en/antibiotics/svarm-reports. Accessed May 26, 2015.

4. Hicks LA, Bartoces MG, Roberts RM, et al. US outpatient antibiotic prescribing variation according to geography, patient population, and provider specialty in 2011. *Clin Infect Dis*. 2015;60(9):1308-1316.

5. Vaz LE, Kleinman KP, Raebel MA, et al. Recent trends in outpatient antibiotic use in children. *Pediatrics*. 2014;133(3):375-385.

6. Suda KJ, Hicks LA, Roberts RM, Hunkler RJ, Taylor TH. Trends and seasonal variation in outpatient antibiotic prescription rates in the United States, 2006 to 2010. *Antimicrob Agents Chemother*. 2014;58(5):2763-2766.

7. Shulman ST, Bisno AL, Clegg HW, et al. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America [published correction appears in *Clin Infect Dis*. 2014;58(10):1496]. *Clin Infect Dis*. 2012;55(10):1279-1282.

8. Lieberthal AS, Carroll AE, Chonmaitree T, et al. The diagnosis and management of acute otitis media [published correction appears in *Pediatrics*. 2014;133(2):346]. *Pediatrics*. 2013;131(3):e964-e999.

9. Chow AW, Benninger MS, Brook I, et al; Infectious Diseases Society of America. IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. *Clin Infect Dis*. 2012;54(8):e72-e112.

10. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical practice guideline (update): adult sinusitis. *Otolaryngol Head Neck Surg*. 2015;152(2)(suppl):S1-S39.

Copyright 2016 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ by Arnab Mukherjee on 03/09/2020

11. Centers for Disease Control and Prevention. Get smart: know when antibiotics work. http://www.cdc.gov/getsmart. Accessed April 12, 2016.

12. The White House. National action plan for combating antibiotic-resistant bacteria. https://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibotic-resistant_bacteria.pdf. Accessed April 12, 2016.

13. Metlay JP. Editorial commentary: setting national targets for antibiotic use. *Clin Infect Dis*. 2015;60(9):1317-1318.

14. Healthy People 2020. Immunization and infectious diseases. https://www.healthypeople.gov/2020/topics-objectives/topic/immunization-and-infectious-diseases/objectives. Accessed October 20, 2015.

15. NCQA. HEDIS 2016. http://www.ncqa.org/HEDISQualityMeasurement/HEDISMeasures/HEDIS2016.aspx. Accessed October 20, 2015.

16. Centers for Disease Control and Prevention. Ambulatory health care data. http://www.cdc.gov/nchs/ahcd.htm. Accessed December 14, 2012.

17. Gonzales R, Malone DC, Maselli JH, Sande MA. Excessive antibiotic use for acute respiratory infections in the United States. *Clin Infect Dis*. 2001;33(6):757-762.

18. Kronman MP, Zhou C, Mangione-Smith R. Bacterial prevalence and antimicrobial prescribing trends for acute respiratory tract infections. *Pediatrics*. 2014;134(4):e956-e965.

19. Shapiro DJ, Hicks LA, Pavia AT, Hersh AL. Antibiotic prescribing for adults in ambulatory care in the United States of America, 2007-09. *J Antimicrob Chemother*. 2014;69(1):234-240.

20. Levri K, Thomas A. Evaluation of Antibiotics Administered for Acute Upper Respiratory Tract Infections—Oregon, 2011. Paper presented at: EIS Conference; April 28, 2014; Atlanta, GA.

21. US Census Bureau, Population Division, Vintage 2010 Special Tabulation and Vintage 2011 Special Tabulation.

22. Shaikh N, Leonard E, Martin JM. Prevalence of streptococcal pharyngitis and streptococcal carriage in children: a meta-analysis. *Pediatrics*. 2010;126(3):e557-e564.

23. Fine AM, Nizet V, Mandl KD. Large-scale validation of the Centor and McIsaac scores to predict group A streptococcal pharyngitis. *Arch Intern Med*. 2012;172(11):847-852.

24. Irwin RS, Baumann MH, Bolser DC, et al; American College of Chest Physicians (ACCP). Diagnosis and management of cough executive summary: ACCP evidence-based clinical practice guidelines. *Chest*. 2006;129(1)(suppl):1S-23S.

25. Hersh AL, Jackson MA, Hicks LA; American Academy of Pediatrics Committee on Infectious Diseases. Principles of judicious antibiotic prescribing for upper respiratory tract infections in pediatrics. *Pediatrics*. 2013;132(6):1146-1154.

26. Ralston SL, Lieberthal AS, Meissner HC, et al; American Academy of Pediatrics. Clinical practice guideline: the diagnosis, management, and prevention of bronchiolitis. *Pediatrics*. 2014;134(5):e1474-e1502.

27. Snow V, Mottur-Pilson C, Gonzales R; American College of Physicians-American Society of Internal Medicine; American Academy of Family Physicians; Centers for Disease Control; Infectious Diseases Society of America. Principles of appropriate antibiotic use for treatment of nonspecific upper respiratory tract infections in adults. *Ann Intern Med*. 2001;134(6):487-489.

28. National Asthma Education and Prevention Program. *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma*. Bethesda, MD: US Dept of Health and Human Services, National Institutes of Health, National Heart, Lung, and Blood Institute; 2007.

29. Fiore AE, Fry A, Shay D, Gubareva L, Bresee JS, Uyeki TM; Centers for Disease Control and Prevention (CDC). Antiviral agents for the treatment and chemoprophylaxis of influenza—recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2011;60(1):1-24.

30. Bradley JS, Byington CL, Shah SS, et al; Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. *Clin Infect Dis*. 2011;53(7):e25-e76.

31. American Academy of Family Physicians; American Academy of Otolaryngology-Head and Neck Surgery; American Academy of Pediatrics Subcommittee on Otitis Media With Effusion. Otitis media with effusion. *Pediatrics*. 2004;113(5):1412-1429.

32. Gupta K, Hooton TM, Naber KG, et al; Infectious Diseases Society of America; European Society for Microbiology and Infectious Diseases. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis*. 2011;52(5):e103-e120.

33. Wald ER, Applegate KE, Bordley C, et al; American Academy of Pediatrics. Clinical practice guideline for the diagnosis and management of acute bacterial sinusitis in children aged 1 to 18 years. *Pediatrics*. 2013;132(1):e262-e280.

34. Gerber JS, Prasad PA, Localio AR, et al. Racial differences in antibiotic prescribing by primary care pediatricians. *Pediatrics*. 2013;131(4):677-684.

35. Centers for Disease Control and Prevention. Get smart know when antibiotics work: measuring outpatient antibiotic prescribing. http://www.cdc.gov/getsmart/community/programs-measurement/measuring-antibiotic-prescribing.html. Accessed February 16, 2016.

36. European Centre for Disease Prevention and Control. Annual epidemiological report 2014: antimicrobial resistance and health care–associated infections. http://ecdc.europa.eu/en/publications/_layouts/forms/Publication_DispForm.aspx?List=4f55ad51-4aed-4d32-b960-af70113dbb90&ID=1292. Accessed April 12, 2016.

37. Groth A, Enoksson F, Hermansson A, Hultcrantz M, Stalfors J, Stenfeldt K. Acute mastoiditis in children in Sweden 1993-2007—no increase after new guidelines. *Int J Pediatr Otorhinolaryngol*. 2011;75(12):1496-1501.

38. Centers for Disease Control and Prevention (CDC). Progress in introduction of pneumococcal conjugate vaccine—worldwide, 2000-2008. *MMWR Morb Mortal Wkly Rep*. 2008;57(42):1148-1151.

39. Drekonja DM, Filice GA, Greer N, et al. Antimicrobial stewardship in outpatient settings: a systematic review. *Infect Control Hosp Epidemiol*. 2015;36(2):142-152.

40. Hing E, Shimizu IM, Talwalkar A. Nonresponse bias in estimates from the 2012 National Ambulatory Medical Care Survey. http://www.cdc.gov/nchs/data/series/sr_02/sr02_171.pdf. Accessed April 12, 2016.

Copyright 2016 American Medical Association. All rights reserved.

Downloaded From: https://jamanetwork.com/ by Arnab Mukherjee on 03/09/2020