Open Forum Infectious Diseases

MAJOR ARTICLE

Prescription Antibiotic Use Among the US population 1999–2018: National Health and Nutrition Examination Surveys

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Background. Antibiotic resistance has been identified as a public health threat both in the United States and globally. The United States published the National Strategy for Combating Antibiotic Resistance in 2014, which included goals to reduce inappropriate outpatient antibiotic use.

Methods. This cross-sectional study was conducted using National Health and Nutrition Examination Surveys (NHANES) years 1999–2018. Weighted prevalence of past 30-day nontopical outpatient antibiotic use was calculated, as well as the change in prevalence from 1999–2002 to 2015–2018 and 2007–2010 to 2015–2018, both overall and for subgroups. Associations with past 30-day nontopical outpatient antibiotic use in 2015–2018 were examined using predictive margins calculated by multivariable logistic regression.

Results. The overall prevalence of past 30-day nontopical outpatient antibiotic use adjusted for age, sex, race/ethnicity, poverty status, time of year of the interview, and insurance status from 1999–2002 to 2015–2018 changed significantly from 4.9% (95% CI, 3.9% to 5.0%) to 3.0% (95% CI, 2.6% to 3.0%), with the largest decrease among children age 0–1 years. From 2007–2010 to 2015–2018, there was no significant change (adjusted prevalence ratio [adjPR], 1.0; 95% CI, 0.8 to 1.2). Age was significantly associated with antibiotic use, with children age 0–1 years having significantly higher antibiotic use than all other age categories >6 years. Being non-Hispanic Black was negatively associated with antibiotic use as compared with being non-Hispanic White (adjPR, 0.6; 95% CI, 0.4 to 0.8).

Conclusions. While there were declines in antibiotic use from 1999–2002 to 2015–2018, there were no observed declines during the last decade.

Keywords. antibiotics; National Health and Nutrition Examination Surveys (NHANES); national trends; United States.

Antibiotic resistance has been identified as a public health threat both in the United States and globally [1]. It is estimated that there are >2.8 million antibiotic-resistant infections each year in the United States alone, causing >35 000 deaths and costing the US health care system ~$20 billion annually [1, 2]. A study using data from the 2010–2011 National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey found that ~30% of all oral antibiotics prescribed during ambulatory visits may have been unnecessary [3]. More recent data suggest that declines since this time have been minimal and vary by age [4]. Despite the prospect of new antibiotics being developed and that appropriately prescribed antibiotics also contribute to resistance, reducing inappropriate antibiotic use is important [1, 3]. The United States White House published the National Strategy for Combating Antibiotic Resistance in 2014, which included goals to reduce inappropriate outpatient antibiotic use by 50% and inappropriate inpatient antibiotic use by 20% by 2020 [5, 6]. Additionally, recent data suggest that broadly distributed antibiotic use (as opposed to intense use from a more limited patient population) and first antibiotic use may more often be associated with antibiotic resistance than repeat use [7].

While insurance claims data are often used to determine trends in prescription medication use, several studies have explored trends in prescription drug use with NHANES data [8–11]. Trends of antibiotic use in the United States using the National Health and Nutrition Examination Survey (NHANES)

Received 5 April 2021; editorial decision 28 April 2021; accepted 29 April 2021.

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Open Forum Infectious Diseases®2021

DOI: 10.1093/ofid/ofab224

were previously published for the years 1999–2012, where Frenk et al. found a significant decline in antibiotic use over the study period [12]. The aim of this study was to describe the trends of past 30-day short-term nontopical antibiotic use in the United States from 1999 to 2018 with a focus on the last decade.

METHODS

Data Source and Population

The NHANES is a cross-sectional, stratified, multistage probability sampling design survey conducted by the National Center for Health Statistics (NCHS). This design allows for the calculation of estimates representative of the noninstitutionalized, civilian US population. The data for NHANES has been collected and released in 2-year intervals since 1999. The survey includes both in-person household interviews and visits to a medical examination center (MEC), where physical examinations, laboratory tests, and audio computer-assisted self-interviews (ACASI) for additional health-related information are performed [13].

Participants who were 16 years or older and emancipated minors answered questions for themselves, while participants 15 years or younger and participants who were unable to answer for themselves had a proxy answer for them [14]. Data for this analysis include NHANES years 1999–2018. All participants who participated in the MEC center portion of the NHANES were included in the analysis.

Prescription Medication Data and Antibiotic Use as an Outcome

All participants were asked during the in-home interview if they had taken any prescription medications in the past 30 days. If the participant had taken a prescription medication in the past 30 days, they provided the name of the medication and how many days they had taken it. All prescription medication data were processed using the Multum Lexicon database. Medication data were provided using the generic drug name [15]. This study included both single- and multi-ingredient drugs that had at least 1 antibiotic listed as an ingredient. This included mostly drugs whose first level category was listed as "anti-infective" but also included a few drugs whose first level category was "gastrointestinal agents" or "genitourinary agents." This analysis did not include antiviral and antifungal medications or antitubuculosis agents and leprostatics. Topical antibiotics (including otic and ophthalmic preparations) were excluded from the majority of the analysis; however, we calculated the use of all antibiotics, which included topical medications, for the study years to visually compare trends with nontopical antibiotic use. All medications included in the analysis are listed in Supplementary Table 1, with variable and value names as provided by the NHANES prescription medication-drug information (RXQ_DRUG) file [15].

If possible, the participant provided the interviewer with the medication container; however, even in cases when the container was not available, the prescription was recorded. This analysis focused on short-term oral antibiotic use; prescriptions were included that were taken for no more than 21 days regardless of whether the medication container was seen by NHANES staff. The medication container was seen in 84.7% of all medications reported (109544/129398), and 67.1% of all reported nontopical antibiotics were used for ≤21 days (2466/3983).

Independent Variables

Demographic variables of interest were asked of all participants during the household interview. Age was categorized into the following groups: 0–1, 2–6, 7–12, 13–17, 18–29, 30–39, 40–49, 50–59, 60+ years. Race/ethnicity was categorized as "Non-Hispanic White," "Non-Hispanic Black," "Mexican American," "Other Hispanic," and "Other Race—Including Multi Racial." Place of birth was defined as having been born in the 50 states or Washington DC or outside the 50 states or Washington DC. The household income's ratio to the federal poverty level was calculated and dichotomized to below the poverty level and at or above the poverty level. Participant sex and insurance status were also considered in the analysis.

Body mass index (BMI) was measured in the MEC and was captured among participants age 2 years and older. Participants age 2 years and older were categorized as "Underweight (<18.5)," "Normal weight (18.5–24.9)," "Overweight (25.0–29.9)," and "Obese (30.0+)." Additionally, participants age 1 year and older were asked whether they had "a head cold or chest cold that started during [the past] 30 days" as well as whether they had "flu, pneumonia, or ear infections that had started during [the past] 30 days." Unfortunately, there was no way to differentiate which infection a participant had specifically experienced. Additionally, these categories were not mutually exclusive. Seasonality was considered using the time of year the interview took place, categorized as either from November 1 to April 30 or from May 1 to Oct 31 by NHANES. Participants age 20 years and older were asked if they had experienced certain comorbidities such as ever having been diagnosed with stroke, cancer/malignancy, diabetes, heart disease (heart failure, coronary heart disease, angina pectoris, or heart attack), lung disease (emphysema or chronic bronchitis), liver disease, or arthritis, as well as if they had an asthma attack/episode of asthma in past 12 months. Participants' number of reported comorbidities were tallied and categorized as 0, 1, or 2+. Missing values for individual comorbidities were imputed as 0 (ie, absent; <0.5% of total observations) for the main analysis.

Statistical Analysis

All statistical analyses were calculated using the MEC weights unless otherwise specified. From 1999 to 2010, the overall unweighted response rate for attending the MEC portion was

>75%. Starting in 2011–2012, the response rate decreased, with an unweighted response rate in 2017–2018 of 48.8% [16]. In addition to considering unequal sampling probabilities for selection, the MEC weights account for nonresponse of both participating in the NHANES as a whole and nonresponse to participating in the MEC.

The overall prevalence rates of past 30-day short-term nontopical antibiotic use and past 30-day short-term all antibiotic use (both topical and nontopical combined) for the 2-year survey intervals were calculated. Additional analyses used survey years grouped into 4-year categories to increase the sample size at each time point to provide more stable estimates; survey weights were adjusted accordingly. The unadjusted prevalence of past 30-day short-term nontopical antibiotic use was calculated both overall and by subgroups of interest for the years 1999–2002, 2007–2010, and 2015–2018. Years were grouped into 4-year intervals to allow for the calculation of stable estimates within subgroups. The change of past 30-day short-term nontopical antibiotic use from 1999–2002 to 2015–2018 and from 2007–2010 to 2015–2018 (average marginal effects) was estimated using the predictive margins calculated from both an unadjusted and adjusted logistic regression accounting for age, sex, race/ethnicity, place of birth, poverty, time of year, and insurance status.

Overall trends in antibiotics use by certain classes of antibiotics (penicillins, cephalosporins, macrolides, and quinolones) were examined. The estimates for prevalence of use for some classes of antibiotics, including sulfonamides, tetracyclines, lincomycins, urinary antinfectives, aminoglycosides, and glycopeptide antibiotics, were unstable as outlined by NCHS standards, and thus were grouped into the "Other" category [17].

Using prevalence ratios (PRs) obtained from the predictive margins estimated by logistic regression, factors associated with past 30-day short-term nontopical antibiotic use in 2015–2018 were examined. A multivariable model was used to calculate adjusted estimates and included the terms age, sex, race, place of birth, poverty status, insurance status, and time of year, as well as the subgroup of interest.

Additionally, in a sensitivity analysis, the proportion of antibiotic use across years was calculated after multiple imputation to account for missingness in the data (~17%–20% of observations missing ≥1 variable per survey period). Missing data are shown in Supplementary Table 2. Continuous variables were imputed using predictive mean matching, while binary variables were imputed using logistic regression. The imputation included all covariates of interest, including education, general health conditions (excellent, very good, good, fair or poor), where participant receives routine health care (clinic or health center, doctor's office or HMO, hospital emergency room, hospital outpatient department, or some other place), number of times in the past year the participant has seen a doctor or health professional (0, 1, 2–3, 4–9, 10–12, 13+), house ownership status, having smoked a cigarette in the past 30 days, and terms for number of smokers in the house. All comorbidities, except asthma and diabetes, were set to 0 for all participants age <20 years for the imputation, but excluded from the analysis using the imputed data. Missing comorbidities that were set to 0 in the main analysis were imputed with multiple imputation by chained equations (MICE). Smoking a cigarette in the past 30 days was imputed to 0 for all participants age <12 years.

Patient Consent

Participants age greater than or equal to 18 years and emancipated minors provided written consent, while participants age 7–17 years provided assent to participate. The analysis was conducted using de-identified publicly available data and was waived from review by the Johns Hopkins University School of Medicine Institutional Review Board.

RESULTS

Trends of Antibiotic Use 1999–2018

The unweighted sample population included 96 766 participants who attended the MEC portion on the NHANES between 1999 and 2018. Of these participants, 81 were missing data on prescription medication use, and therefore were excluded from the main analysis, but were included in the MICE sensitivity analysis. In 2017–2018, past 30-day short-term nontopical use was 3.2% (95% CI, 2.5% to 4.0%), down from 4.6% (95% CI, 3.7% to 5.6%) in 1999–2000 (Figure 1). Past 30-day short-term antibiotic use for all antibiotics (both topical and nontopical) from 1999 to 2018 followed the same trend as past 30-day short-term nontopical use over the same years.

The prevalence of past 30-day short-term nontopical use decreased significantly from 1999–2002 to 2015–2018 (adjusted prevalence ratio [aPR], 0.7; 95% CI, 0.5 to 0.8) (Table 1) adjusting for age, sex, race/ethnicity, poverty status, place of birth, time of year, and insurance status. Among the different age categories, decreases were seen in children age 0–1 years (aPR, 0.6; 95% CI, 0.3 to 0.8), as well as people in the following age categories: 6–11, 12–17, and 18–39 years. Additionally during this time period, there was a decrease in antibiotic use among non-Hispanic White, Mexican American, and other Hispanic populations, as well as among people born in the 50 US states and Washington DC. There was no significant decrease in antibiotic use among the non-Hispanic Black population, those categorized as other race/multiracial, or people born outside of the United States, although the trends in these groups were similar to those in other groups. Decreases were seen both among people below the poverty line and among those at or above the poverty line; however, the magnitude of decrease was slightly larger among those below the poverty line.

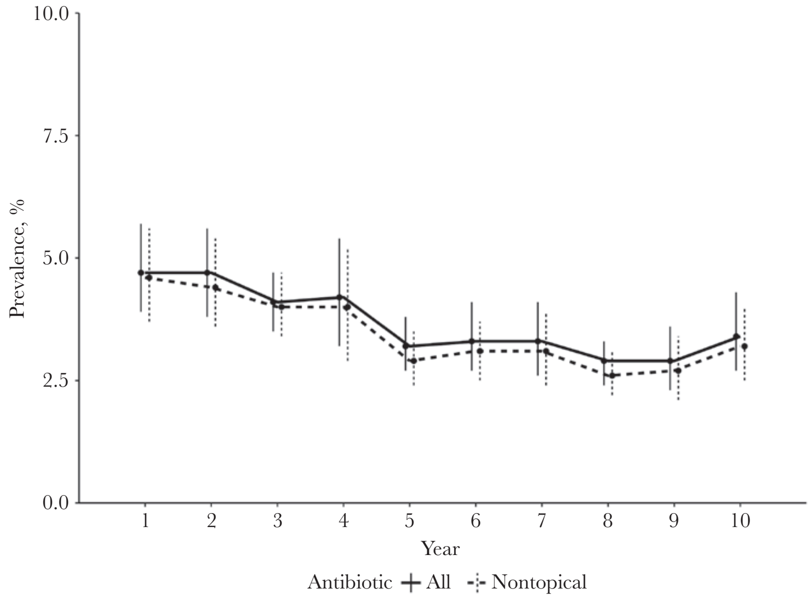

Figure 1. Prevalence of past 30-day antibiotic use from 1999 to 2018 among the US population in the National Health and Nutrition Examination Surveys. All data are weighted prevalence estimates using Medical Examination Center survey weights provided by the National Center for Health Statistics with corresponding Korn and Graubard 95% CIs.

In addition to general sociodemographic factors, prevalence of antibiotic use significantly decreased both among people who not diagnosed with a head or chest cold over the past 30 days (aPR, 0.6; 95% CI, 0.5 to 0.8). While short-term antibiotic use among those who had flu pneumonia or an ear infection over the past 30 days did not change, antibiotic use significantly decreased among those who did not report these infections (aPR, 0.7; 95% CI, 0.5 to 0.8). Additionally, the significant decrease among participants who were interviewed from November 1 to April 30 was similar to the decrease of those who were interviewed from May 1 to October 31.

Importantly, from 2007–2010 to 2015–2018, there was no significant change (aPR, 1.0; 95% CI, 0.8 to 1.2) in short-term antibiotic use. While the non-Hispanic Black population and the uninsured population saw a decrease in univariate analysis during these years, these decreases were no longer significant after adjustment. After multiple imputation to account for missing data, the trends generally remained the same (Supplementary Table 3).

Trends of Antibiotic Use 1999–2018 by Class

The most commonly used class of antibiotics was penicillins (Table 2), which accounted for nearly half of all antibiotic use in all years. Amoxicillin made up of the majority of all penicillin use in all years. There was a significant decrease in the use of penicillins (PR, 0.6; 95% CI, 0.5 to 0.8) and cephalosporins (PR, 0.6; 95% CI, 0.5 to 0.9) from 1999–2002 to 2015–2018. However, like overall antibiotic use, there were no decreases observed from 2007–2010 to 2015–2018 in any class or type of antibiotic.

Factors Associated With Antibiotic Use Between 2015 and 2018

Associations with antibiotic use in 2015–2018 are shown in Table 3. Age was significantly associated with antibiotic use, with children age 0–1 years having significantly higher antibiotic use than all other age categories. Being non-Hispanic Black was negatively associated with antibiotic use as compared with being non-Hispanic White (adjPR, 0.6; 95% CI, 0.4 to 0.8). While time of year was not significantly associated with antibiotic use in a univariate analysis, after adjustment for confounders, those who were interviewed between November 1 and April 30 were significantly more likely to have been on antibiotics during the past 30 days than those who were interviewed between May 1 and October 30. Having a head or chest cold in the past 30 days remained significant after adjustment for confounders, as well as having the flu, pneumonia, or an ear infection in the past 30 days. Being overweight or obese was significantly associated with lower use of antibiotics as compared with being underweight.

DISCUSSION

In this analysis of nationally representative data, there was a significant decrease in antibiotic use from 1999–2000 to 2015–2018, but no change from 2007–2010 to 2015–2018, suggesting that the largest decrease in antibiotic use over the past 2 decades took place during the earlier years.

Barriers to appropriate antibiotic prescribing among physicians include providers' perceptions of patients' expectations of treatment and patient's knowledge levels regarding antibiotic resistance, although a recent study from Australia

Table 1. Past 30-Day Nontopical Outpatient Antibiotic Use From 1999 to 2018 Among the US Population

	1999–2002	2007–2010	2015–2018	1999–2002 vs 2015–2018	1999–2002 vs 2015–2018	2007–2010 vs 2015–2018	2007–2010 vs 2015–2018
Characteristics	Prevalence, % (95% CI)	Prevalence, % (95% CI)	Prevalence, % (95% CI)	PR (95% CI)	aPR (95% CI)[a]	PR (95% CI)	aPR (95% CI)[a]
Overall	4.9 (3.9 to 5.0)	3.0 (2.6 to 3.0)	3.0 (2.5 to 3.0)	0.7 (0.5 to 0.8)	0.7 (0.5 to 0.8)	1.0 (0.8 to 1.2)	1.0 (0.8 to 1.2)
Age							
0–1	14.9 (11.7 to 18.6)	11.5 (8.7 to 14.7)	8.8 (6.2 to 12.0)	0.6 (0.4 to 0.8)	0.6 (0.3 to 0.8)	0.8 (0.5 to 1.1)	0.8 (0.4 to 1.1)
2–5	8.7 (6.8 to 11.0)	6.6 (4.5 to 9.3)	5.7 (3.5 to 8.5)	0.6 (0.3 to 1.0)	0.7 (0.3 to 1.0)	0.9 (0.4 to 1.3)	0.9 (0.4 to 1.4)
6–11	5.8 (4.0 to 8.1)	4.3 (3.2 to 5.7)	3.2 (2.1 to 4.8)	0.6 (0.3 to 0.8)	0.5 (0.3 to 0.8)	0.8 (0.4 to 1.1)	0.7 (0.4 to 1.0)
12–17	5.3 (3.9 to 7.0)	3.4 (2.0 to 5.5)	2.6 (1.6 to 3.9)	0.5 (0.2 to 0.7)	0.5 (0.2 to 0.8)	0.8 (0.3 to 1.2)	0.8 (0.3 to 1.3)
18–39	4.3 (3.2 to 5.7)	2.9 (2.2 to 3.8)	2.5 (1.9 to 3.3)	0.6 (0.4 to 0.8)	0.6 (0.3 to 0.8)	0.9 (0.5 to 1.2)	0.8 (0.5 to 1.1)
40–59	3.4 (2.6 to 4.4)	2.1 (1.6 to 2.7)	3.1 (2.3 to 4.2)	0.9 (0.6 to 1.3)	1.0 (0.6 to 1.3)	1.5 (0.9 to 2.1)	1.4 (0.9 to 2.0)
60+	2.2 (1.6 to 3.1)	1.2 (0.9 to 1.6)	2.1 (1.4 to 3.0)	0.9 (0.5 to 1.4)	1.0 (0.5 to 1.5)	1.7 (0.9 to 2.5)	2.0 (0.9 to 3.1)
Sex							
Male	4.0 (3.3 to 4.9)	2.9 (2.3 to 3.5)	2.8 (2.1 to 3.7)	0.7 (0.5 to 0.9)	0.7 (0.5 to 0.9)	1.0 (0.7 to 1.3)	1.0 (0.7 to 1.3)
Female	4.9 (4.3 to 5.6)	3.1 (2.7 to 3.6)	3.1 (2.5 to 3.7)	0.6 (0.5 to 0.8)	0.7 (0.5 to 0.8)	1.0 (0.8 to 1.2)	1.0 (0.8 to 1.3)
Race/ethnicity							
Non-Hispanic White	5.0 (4.2 to 5.9)	3.1 (2.6 to 3.7)	3.3 (2.7 to 4.1)	0.7 (0.5 to 0.8)	0.7 (0.5 to 0.8)	1.1 (0.8 to 1.3)	1.0 (0.8 to 1.3)
Non-Hispanic Black	3.0 (2.3 to 3.8)	2.6 (2.1 to 3.2)	1.8 (1.3 to 2.4)	0.6 (0.4 to 0.8)	0.7 (0.4 to 1.0)	0.7 (0.4 to 0.9)	0.7 (0.5 to 1.0)
Mexican American	3.9 (3.2 to 4.7)	3.1 (2.3 to 4.1)	2.5 (1.8 to 3.4)	0.6 (0.4 to 0.9)	0.7 (0.4 to 0.9)	0.8 (0.5 to 1.1)	0.8 (0.4 to 1.1)
Other Hispanic	4.7 (3.7 to 5.8)	2.7 (1.9 to 3.6)	2.8 (1.9 to 3.8)	0.6 (0.4 to 0.8)	0.6 (0.3 to 0.8)	1.0 (0.6 to 1.5)	1.2 (0.6 to 1.8)
Other race—including multiracial	2.4 (1.4 to 3.8)	2.4 (1.6 to 3.4)	2.6 (1.8 to 3.7)	1.1 (0.4 to 1.7)	1.2 (0.5 to 1.9)	1.1 (0.5 to 1.6)	1.2 (0.5 to 1.9)
Place of birth							
Born in 50 states or Washington DC	4.8 (4.2 to 5.5)	3.2 (2.8 to 3.7)	3.2 (2.7 to 3.7)	0.7 (0.5 to 0.8)	0.7 (0.5 to 0.8)	1.0 (0.8 to 1.2)	1.0 (0.8 to 1.2)
Born outside 50 states or Washington DC	2.3 (1.5 to 3.5)	1.7 (1.2 to 2.4)	1.7 (1.0 to 2.9)	0.7 (0.3 to 1.2)	0.8 (0.2 to 1.4)	1.0 (0.4 to 1.6)	1.0 (0.3 to 1.7)
Poverty status							
Below the poverty level	4.6 (3.4 to 5.9)	3.6 (3.0 to 4.3)	2.7 (2.0 to 3.6)	0.6 (0.4 to 0.8)	6 (0.4 to 0.8)	0.8 (0.5 to 1.0)	0.6 (0.2 to 1.0)
At or above poverty level	4.6 (4.0 to 5.3)	2.9 (2.5 to 3.4)	3.1 (2.6 to 3.7)	0.7 (0.5 to 0.8)	0.7 (0.5 to 0.9)	1.1 (0.8 to 1.3)	1.1 (0.8 to 1.3)
Insurance status							
Not insured	3.4 (2.2 to 5.1)	2.5 (1.9 to 3.1)	1.4 (0.8 to 2.3)	0.4 (0.1 to 0.7)	0.5 (0.2 to 0.8)	0.6 (0.2 to 0.9)	1.0 (0.7 to 1.3)
Insured	4.7 (4.0 to 5.5)	3.1 (2.6 to 3.6)	3.1 (2.7 to 3.7)	0.7 (0.5 to 0.8)	0.7 (0.5 to 0.9)	1.0 (0.8 to 1.2)	1.0 (0.6 to 1.3)
BMI[b]							
Underweight (<18.5)	6.6 (5.3 to 8.0)	4.6 (3.3 to 6.1)	4.5 (3.5 to 5.6)	0.7 (0.5 to 0.9)	0.6 (0.5 to 0.8)	1.0 (0.6 to 1.3)	1.0 (0.7 to 1.2)
Normal weight (18.5–24.9)	4.1 (3.3 to 5.0)	3.0 (2.3 to 3.8)	3.3 (2.3 to 4.5)	0.8 (0.5 to 1.1)	0.9 (0.6 to 1.1)	1.1 (0.7 to 1.6)	1.1 (0.8 to 1.5)
Overweight (25.0–29.9)	3.7 (3.0 to 4.6)	2.1 (1.5 to 2.8)	2.2 (1.5 to 3.1)	0.6 (0.4 to 0.8)	0.7 (0.4 to 0.9)	1.0 (0.6 to 1.5)	1.0 (0.6 to 1.3)
Obese (30.0+)	3.5 (2.7 to 4.4)	2.3 (1.9 to 2.7)	2.2 (1.7 to 2.7)	0.6 (0.4 to 0.8)	0.8 (0.5 to 1.1)	1.0 (0.7 to 1.2)	1.1 (0.7 to 1.5)
Head or chest cold past 30 d[c]							
No	3.5 (3.0 to 4.0)	2.3 (1.9 to 2.7)	2.1 (1.7 to 2.6)	0.6 (0.5 to 0.8)	0.6 (0.4 to 0.8)	0.9 (0.7 to 1.2)	1.0 (0.7 to 1.2)
Yes	7.8 (6.3 to 9.5)	6.1 (4.9 to 7.5)	6.5 (5.0 to 8.4)	0.8 (0.6 to 1.1)	0.9 (0.6 to 1.1)	1.1 (0.7 to 1.4)	1.1 (0.8 to 1.5)

Table 1. Continued

Characteristics	1999–2002	2007–2010	2015–2018	1999–2002 vs 2015–2018	1999–2002 vs 2015–2018	2007–2010 vs 2015–2018	2007–2010 vs 2015–2018
	Prevalence, % (95% CI)	Prevalence, % (95% CI)	Prevalence, % (95% CI)	PR (95% CI)	aPR (95% CI)[a]	PR (95% CI)	aPR (95% CI)[a]
Flu, pneumonia, ear infection past 30 d[c]							
No	3.8 (3.3 to 4.5)	2.5 (2.2 to 2.9)	2.5 (2.1 to 2.9)	0.6 (0.5 to 0.8)	0.7 (0.5 to 0.8)	1.0 (0.8 to 1.2)	1.0 (0.8 to 1.2)
Yes	15.1 (12.4 to 18.1)	13.3 (10.0 to 17.2)	13.7 (9.8 to 18.3)	0.9 (0.6 to 1.2)	1.1 (0.7 to 1.5)	1.0 (0.6 to 1.4)	1.2 (0.7 to 1.6)
Time of year interview conducted							
November 1–April 30	5.7 (4.8 to 6.7)	3.5 (2.9 to 4.2)	3.5 (2.8 to 4.3)	0.6 (0.4 to 0.8)	0.6 (0.5 to 0.8)	0.6 (0.5 to 0.8)	1.0 (0.7 to 1.3)
May 1–October 31	3.7 (3.2 to 4.4)	2.6 (2.1 to 3.2)	2.5 (1.9 to 3.3)	0.7 (0.5 to 0.9)	0.7 (0.5 to 0.9)	1.0 (0.6 to 1.3)	.01 (0.6 to 1.3)
No. of comorbidities[d]							
0	3.3 (2.6 to 4.1)	2.3 (1.8 to 2.8)	2.8 (2.1 to 3.5)	0.8 (0.6 to 1.1)	0.8 (0.6 to 1.1)	1.2 (0.8 to 1.6)	1.1 (0.8 to 1.5)
1	3.7 (2.5 to 5.1)	2.1 (1.5 to 2.7)	2.2 (1.4 to 3.3)	0.6 (0.3 to 0.9)	0.6 (0.3 to 1.0)	1.1 (0.5 to 1.6)	1.2 (0.6 to 1.8)
2	3.9 (2.8 to 5.3)	1.8 (1.2 to 2.6)	2.7 (1.8 to 3.9)	0.7 (0.4 to 1.0)	0.8 (0.4 to 1.1)	1.5 (0.7 to 2.3)	1.7 (0.7 to 2.6)

All data are weighted prevalence estimates using Medical Examination Center survey weights provided by the National Center for Health Statistics with corresponding Korn and Graubard 95% CIs.

Abbreviations: aPR, adjusted prevalence ratio; BMI, body mass index; PR, prevalence ratio.

[a]Adjusted for age, sex, race, place of birth, poverty, insurance status, time of year.

[b]Two years and older.

[c]One year and older.

[d]Twenty years and older; comorbidities include stroke, cancer/malignancy, diabetes, heart disease (heart failure, coronary heart disease, angina pectoris, or heart attack), lung disease (emphysema or chronic bronchitis), liver disease, or arthritis, as well as if they had an asthma attack/episode of asthma in past 12 months.

Table 2. Past 30-Day Nontopical Antibiotic Use by Type of Antibiotic, NHANES 1999–2018

	1999–2002	2007–2010	2015–2018	1999–2002 vs 2015–2018	2007–2010 vs 2015–2018
	Prevalence, % (95% CI)	Prevalence, % (95% CI)	Prevalence, % (95% CI)	PR (95% CI)	PR (95% CI)
Nontopical	4.5 (3.9 to 5.1)	3.0 (2.6 to 3.4)	3.0 (2.5 to 3.4)	0.7 (0.5 to 0.8)	1.0 (0.8 to 1.2)
Penicillins	2.2 (1.9 to 2.6)	1.4 (1.1 to 1.6)	1.4 (1.1 to 1.7)	0.6 (0.5 to 0.8)	1.0 (0.7 to 1.3)
Cephalosporins	0.8 (0.6 to 1.0)	0.5 (0.4 to 0.7)	0.5 (0.4 to 0.7)	0.6 (0.4 to 0.9)	1.0 (0.6 to 1.4)
Macrolides	0.7 (0.5 to 1.0)	0.4 (0.3 to 0.6)	0.5 (0.3 to 0.8)	0.7 (0.3 to 1.1)	1.2 (0.5 to 1.9)
Quinolones	0.3 (0.2 to 0.4)	0.3 (0.2 to 0.5)	0.2 (0.1 to 0.4)	0.9 (0.2 to 1.5)	0.8 (0.2 to 1.3)
Other[a]	0.2 (0.1 to 0.3)	0.2 (0.1 to 0.3)	0.2 (0.1 to 0.3)	0.0 (–0.2 to 0.1)	0.0 (–0.2 to 0.1)
Topical	0.3 (0.2 to 0.4)	0.3 (0.2 to 0.5)	0.3 (0.2 to 0.4)	0.9 (0.3 to 1.5)	0.9 (0.2 to 1.6)
Individual					
Amoxicillin	2.0 (1.6 to 2.4)	1.2 (1.0 to 1.5)	1.3 (1.0 to 1.6)	0.6 (0.5 to 0.8)	1.1 (0.7 to 1.4)
Cephalexin	0.4 (0.3 to 0.6)	0.3 (0.2 to 0.4)	0.3 (0.2 to 0.4)	0.6 (0.3 to 0.9)	1.0 (0.4 to 1.5)
Azithromycin	0.3 (0.2 to 0.5)	0.3 (0.2 to 0.5)	0.4 (0.2 to 0.7)	1.4 (0.5 to 2.4)	1.3 (0.5 to 2.1)

All data are weighted prevalence estimates using Medical Examination Center survey weights provided by the National Center for Health Statistics with corresponding Korn and Graubard 95% CIs.

Abbreviations: NHANES, National Health and Nutrition Examination Surveys; PR, prevalence ratio.

[a]Sulfonamides, tetracyclines, lincomycins, urinary antinfectives, urinary antispasmotics that include an ingredient identified as an anti-infective, miscellaneous, aminoglycosides, glycopeptide antibiotics.

Table 3. Associations With Past 30-Day Nontopical Outpatient Antibiotic Use Among the US Population 2015–2018

Characteristic	Prevalence Ratio	Adjusted Prevalence Ratio[a]
Age		
0–1	1	1
2–5	0.6 (0.3 to 1.0)	0.7 (0.3 to 1.0)
6–11	0.4 (0.2 to 0.5)	0.4 (0.2 to 0.5)
12–17	0.3 (0.2 to 0.4)	0.3 (0.2 to 0.4)
18–39	0.3 (0.2 to 0.4)	0.3 (0.2 to 0.4)
40–59	0.4 (0.2 to 0.5)	0.4 (0.2 to 0.5)
60+	0.2 (0.1 to 0.4)	0.2 (0.1 to 0.4)
Sex		
Male	1	1
Female	1.1 (0.7 to 1.4)	1.1 (0.7 to 1.5)
Race/ethnicity		
Non-Hispanic White	1	1
Non-Hispanic Black	0.5 (0.4 to 0.7)	0.6 (0.4 to 0.8)
Mexican American	0.8 (0.5 to 1.0)	0.7 (0.5 to 1.0)
Other Hispanic	0.8 (0.5 to 1.1)	0.9 (0.5 to 1.3)
Other race—including multiracial	0.8 (0.5 to 1.1)	0.8 (0.4 to 1.3)
Place of birth		
Born in 50 states or Washington DC	1	1
Born outside 50 states or Washington DC	0.5 (0.2 to 0.9)	0.7 (0.1 to 1.3)
Poverty status		
Below the poverty level	1	1
At or above poverty level	1.1 (0.8 to 1.5)	1.1 (0.8 to 1.4)
Insurance status		
Not insured	1	1
Insured	2.2 (1.0 to 3.5)	1.8 (0.7 to 3.0)
BMI[b]		
Underweight (<18.5)	1	1
Normal weight (18.5–24.9)	0.7 (0.5 to 1.0)	0.8 (0.6 to 1.0)
Overweight (25.0–29.9)	0.5 (0.3 to 0.7)	0.6 (0.3 to 0.9)
Obese (30.0+)	0.5 (0.3 to 0.7)	0.5 (0.1 to 0.9)
Head or chest cold past 30 d[c]		
No	1	1
Yes	3.1 (2.0 to 4.2)	2.8 (1.7 to 3.9)
Flu, pneumonia, ear infection past 30 d[c]		
No	1	1
Yes	5.6 (3.6 to 7.5)	5.5 (3.3 to 7.6)
Time of year interview conducted		
November 1–April 30	1	1
May 1–October 31	0.7 (0.4 to 1.0)	0.7 (0.4 to 0.9)
No. of comorbidities[d]		
0	1	1
1	0.8 (0.4 to 1.2)	1.0 (0.7 to 1.3)
2	1.0 (0.5 to 1.4)	1.0 (0.4 to 1.6)

Crude prevalence ratios (average marginal effect of each category) and corresponding 95% CIs were estimated from survey-weighted univariable logistic regression.

Abbreviation: BMI, body mass index.

[a]Adjusted prevalence ratios (average marginal effect of each category) and corresponding 95% CIs in antibiotic use prevalence were estimated by survey-weighted multivariable logistic regression models including age, sex, race, place of birth, poverty status, insurance status time of year, having a head chest or chest cold in the last 30 days, and having been diagnosed with flu, pneumonia, or an ear infection in the past 30 days.

[b]Two years and older.

[c]One year and older.

[d]Twenty years and older; comorbidities include stroke, cancer/malignancy, diabetes, heart disease (heart failure, coronary heart disease, angina pectoris, or heart attack), lung disease (emphysema or chronic bronchitis), liver disease, or arthritis, as well as if they had an asthma attack/episode of asthma in past 12 months.

that interviewed both general practitioners and caregivers of children <5 years of age found that practitioners may overestimate the importance of prescribing antibiotics for young children based on a perceived notion of parent satisfaction and knowledge [18–20]. Another study suggested that providers may externalize blame and responsibility to prescribers other than themselves for antibiotic resistance and its management [21]. In addition, the 7-valent and 13-valent pneumococcal conjugate vaccines were introduced in early 2000, which reduced the incidence of vaccine-type invasive pneumococcal disease and could have led to a reduction in antibiotic use [12, 22, 23].

The findings of this study are consistent with previously published data of earlier years. The subgroup results are similar to the previous NHANES study by Frenk et al. examining antibiotic use trends between years that showed the largest absolute decline in children under 2 years of age [12]. However, this subgroup also had the highest overall antibiotic use prevalence to begin with, and the relative prevalence difference was not of greater magnitude than age groups from 6 to 39 years, which also saw a significant decline. A study by King et al. evaluated trends in antibiotic use from community pharmacy dispensing data and found a decline from 2011 to 2014, with a plateau in 2015–2016 [24]. While we did not calculate the change from 2011–2012 to 2015–2016 and the associated statistical significance, we found similar trends for these years, which demonstrates that this trend is consistent across data sources. This study also found that younger age and having a head/chest cold in the past 30 days were positively associated with antibiotic use, consistent with other studies that infants and young children have the highest rates of antibiotic use [25, 26]. Non-Hispanic Black race was negatively associated with antibiotic use, which is likely attributable to the prevalence of racial disparities in prescribing practices, which has been previously documented, and health care in general [27, 28]. Surprisingly, there was no association between insurance status and antibiotic use.

There are limitations with this study. One limitation is that antibiotic use was collected by self-report. While all prescription data were collected for medications used within 30 days before the interview—which hypothetically would have less recall bias as compared with medications used in the past before the interview—there was still the potential for participants to not remember whether they took a prescription medication or which prescription they took, especially in the case where the participant was no longer in possession of the medication bottle. Additionally, as prescription medication use was only collected for the 30 days before the interview, this study only allows for the estimation of past 30-day use of antibiotics and not total use over the year. Compared with pharmacy claims data, the data set provided by NHANES is relatively small, which may have restricted our ability to detect smaller yet still meaningful decreases. Unfortunately, there were no data collected regarding where the prescription was issued, so trends regarding prescription location could not be estimated. Lastly, the response rate to NHANES decreased over time, which has the potential to bias estimates. However, one strength of this study is that NHANES provides nationally representative estimates. Additionally, NHANES gathers consistent information on a wide variety of demographic and personal characteristics that allow for exploration of trends and associations among various subgroups of interest, including uninsured people.

Overall, these data suggest that, despite the push for antimicrobial stewardship and reducing unnecessary antimicrobial prescriptions, the progress of reduction over the past decade may be slower than desired. Further investigation should be conducted for the most recent years to verify if these findings hold across data sources, as this would imply that the United States has not met the goals established in 2014 to reduce antibiotic use [5]. Studies have also shown that antibiotic prescribing in the United States differs by region [26, 29]. While the need for antibiotic stewardship is evident, there are many gaps in the research on achieving and sustaining appropriate antibiotic prescribing for a wide range of geographic and clinical settings and employing the expertise of various disciplines and stakeholders [30, 31]. Additionally, technologies or improved antibiotic use guidelines that improve the diagnostic capabilities of clinicians, as well as vaccines that target antimicrobial-nonsusceptible organisms, may help improve outcomes [23, 32–35]. It is also important to re-engage physicians in the United States as well as the general public to reach the goals of reducing antibiotic use.

Supplementary Data

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

Acknowledgments

The authors are grateful to the NHANES study staff and participants, without whom this study would not have been possible.

Financial support. This work was supported in part by National Institute of Allergy and Infectious Diseases (NIAID) extramural support (R01AI120938 and R01AI128779 to A.A.R.T.; and T32AI102623 to E.U.P.) and the NIAID Division of Intramural Research (T.C.Q.)

Potential conflicts of interest. All authors: no reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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