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Trends in the use of prescription antibiotics: NHANES 1999–2012

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Abstract

Objectives: The objectives of this study were: to examine trends in the use of prescription antibiotics overall and by population subgroups between 1999 and 2012; and to examine trends in the use of categories of antibiotics and individual antibiotics.

Methods: Use of antibiotics was examined among 71444 participants in the nationally representative National Health and Nutrition Examination Survey (NHANES; 1999–2012). Use of an antibiotic in the past 30 days was the main outcome variable. Analyses of trends were conducted overall and separately by population subgroups (i.e. age, sex, race/Hispanic origin, health insurance status and respiratory conditions) across four time periods (1999–2002, 2003–06, 2007–10 and 2011–12).

Results: The percentage of the US population that used a prescription antibiotic in the past 30 days significantly declined from 6.1% in 1999–2002 to 4.1% in 2011–12 ($P < 0.001$). Declines were also identified for five age groups (0–1 year, 6–11 years, 12–17 years, 18–39 years and 40–59 years), both sexes, non-Hispanic white and non-Hispanic black persons, persons with and without insurance and among those who currently had asthma. Significant declines were also observed for three categories of antibiotics (penicillins, cephalosporins and macrolide derivatives). Of the most common antibiotics prescribed, only amoxicillin use decreased significantly.

Conclusions: Overall, there was a significant decline in the use of antibiotics between 1999–2002 and 2011–12. Due to concerns about antimicrobial resistance, it is important to continue monitoring the use of antibiotics.

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Author contributions

S. M. F.: study concept and design; acquisition, analysis or interpretation of data; drafting of the manuscript; statistical analysis. B. K. K.: study concept and design; acquisition, analysis or interpretation of data; critical revision of the manuscript for important intellectual content; administrative, technical or material support. S. L. L.: study concept and design; acquisition, analysis or interpretation of data; critical revision of the manuscript for important intellectual content; administrative, technical or material support. L. A. H.: study concept and design; acquisition, analysis or interpretation of data; critical revision of the manuscript for important intellectual content; administrative, technical or material support. Q. G.: acquisition, analysis or interpretation of data; critical revision of the manuscript for important intellectual content; administrative, technical or material support.

Transparency declarations

None to declare.

Introduction

Antimicrobial resistance threatens health professionals' ability to effectively treat infectious diseases. Inappropriate use of antibiotics contributes to the development of antimicrobial resistance, which leads to drug-resistant bacterial infections. At the individual level, these infections can lead to serious illness or death, and at the macro level they place undue burden on the healthcare system.^{2,4,5}

Reporting of antibiotic prescribing in the USA has previously been based on analyses of pharmacy dispensing data (including the IMS Health Xponent database) or data from the National Ambulatory Medical Care Survey (NAMCS) and the National Hospital Ambulatory Medical Care Survey (NHAMCS). These studies have shown an overall decline in antibiotic prescribing by office-based physicians and hospital emergency and outpatient departments during the 1990s and early 2000s."

Data from the National Health and Nutrition Examination Survey (NHANES) can build on these studies and provide more details about trends in the use of antibiotics. NHANES collects information about prescription medication use from a nationally representative sample of the US non-institutionalized population through direct observation of medication containers in the home or by self- and proxy-reported medication use. The study also collects detailed information about people's demographic characteristics and their health, which can allow researchers to examine trends in antibiotic use among population subgroups.

In this study, we examined trends in the use of antibiotics overall and by population subgroups between 1999–2002 and 2011–12 using NHANES data. We also examined trends in the use of categories of antibiotics and individual antibiotics.

Methods

Data

Data for this analysis come from the NHANES, a continuous, crosssectional survey conducted by the National Center for Health Statistics (NCHS), CDC. A complex, multistage probability sampling design was used to generate a representative sample of the civilian, non-institutionalized US population. Survey participants received a detailed in-home interview followed by a physical examination at a mobile examination centre. Study protocols were approved by NCHS's Research Ethics Review Board. Informed consent was obtained from participants aged ≥ 18 years. For those younger than 18 years, written parental consent was obtained and children's assent was also obtained for those aged 7–17 years. Since 1999, data were collected on an annual basis, but released in 2 year cycles. To generate reliable estimates, data from all available cycles were combined into three 4 year time periods (1999–2002, 2003–06 and 2007–10) and one 2 year period (2011–12). The overall interview response rate was 83% in 1999–2002, 80% in 2003–06, 79% in 2007–10 and 73% in 2011–12. The analytical sample included all NHANES respondents who completed the household interview and had complete information on their use of prescription medication ($n = 71444$).

Variables

Data on prescription medications used in the past 30 days were collected through direct abstraction from prescription medication containers. During the household interview, respondents aged ≥ 16 years were asked: ‘In the past 30 days, have you used or taken medication for which a prescription is needed?’ For respondents under the age of 16 or those that could not respond to the question, a proxy responded. Those who answered affirmatively were asked to give their prescription medication containers to the interviewer and report details related to its use (i.e. duration of use). An interviewer took the container and recorded the exact product name from its label. If the container was not available, the participant verbally reported this information. In most instances, interviewers saw the medicine container for each antibiotic used (70% of antibiotic containers in 1999–2002, 76% in 2003–06, 70% in 2007–10 and 72% in 2011–12). Collection methodology was similar for all NHANES cycles. Further details of prescription medication data collection in NHANES 1999–2012 are available elsewhere.

All the drug names reported were converted into a standard generic drug name for the data release and a therapeutic drug class was assigned based on the Multum Lexicon Drug Database. To generate a dichotomous variable indicating that a respondent had taken an antibiotic in the past 30 days, we examined all drugs within the first-level category, ‘anti-infectives’, and excluded drugs that were not antibiotics. Topical antibiotics were also excluded from the analysis. We also generated variables to assess trends in the use of different categories of antibiotics using the second-level drug categories from the Multum Lexicon Drug Database. We also examined trends in the use of the three most frequently used antibiotics among survey respondents: amoxicillin, azithromycin and cefalexin.

In addition to examining the overall trend in antibiotic use, we examined trends among several subpopulations, including: age groups (0–1 year, 2–5 years, 6–11 years, 12–17 years, 18–39 years, 40–59 years and ≥ 60 years), self-identified race/Hispanic origin (non-Hispanic black, non-Hispanic white, Mexican American and other), sex (male and female), health insurance status (have health insurance and do not have health insurance). Respiratory tract infections (acute and chronic) are a leading indication for antibiotic prescribing in the ambulatory setting, and the use of antibiotics among people with these infections has been examined in prior research.¹⁰ NHANES data do not contain information on acute respiratory tract infections; however, we were able to examine antibiotic use among individuals with chronic respiratory conditions. This included persons who currently had asthma and persons who were ever told by their doctor they had emphysema and/or who currently had chronic bronchitis.

Statistical analysis

Statistical analyses were conducted using the survey (SVY) commands in Stata 12.1 to adjust for differential probabilities of selection and the complex sampling design. Interview sample weights were used to obtain estimates representative of the civilian, non-institutionalized US population. Variance estimates were computed using the Taylor series linearization approximation method. CIs were calculated using a logit transformation based on the estimated standard errors. Antibiotic use estimates for the race/Hispanic origin groups

were age standardized to the projected estimates of the 2000 US Census by the direct method, using seven age groups: 0–1 year, 2–5 years, 6–11 years, 12–17 years, 18–39 years, 40–59 years and 60 years. Estimates with a relative standard error .30% were considered statistically unreliable and noted in tables.

We generated estimates of the percentage of the US non-institutionalized population who used an antibiotic in the past 30 days overall and among the subpopulations mentioned above. In addition, we examined trends in the use of different categories of antibiotics and three individual antibiotics. We tested for the presence of linear trends using orthogonal contrast matrices generated using Stata's 'contrast' command, adjusted for the uneven midpoints of the time periods used in the analysis (three 4 year periods and one 2 year period). For all tests, a significance level of 0.05 was utilized. We also reported the absolute change in percentage between the first and last time periods examined (i.e. 1999–2002 and 2011–12).

Results

The percentage of the US population that used a prescription antibiotic in the past 30 days declined significantly from 6.1% in 1999–2002 to 4.1% in 2011–12 (Table 1). Significant declines in the use of antibiotics were found among many of the subpopulations examined, although the magnitude of the declines varied. There were significant declines in the use of antibiotics among five of the seven age groups examined: children aged 0–1 year, children aged 6–11 years, teenagers aged 12–17 years, adults aged 18–39 years and adults aged 40–59 years. The magnitude of the changes ranged from 1.3% to 6.8%. The biggest decline was among the youngest age group (children aged 0–1 year), in which the percentage declined by almost half between 1999–2002 and 2011–12 (from 15.5% to 8.7%).

A significant decline in antibiotic use occurred for both males and females. The magnitude of the decline was greater for males (2.4%) compared with females (1.6%), and in the most recent period examined females continued to use more antibiotics than males (4.9% compared with 3.2%). Use of antibiotics declined among non-Hispanic white and non-Hispanic black persons; however, their use remained relatively stable among Mexican American persons. The decline was greater among non-Hispanic white persons compared with non-Hispanic black persons (2.0% compared with 1.2%).

Use of antibiotics declined among persons with health insurance and those without health insurance. The magnitude of the decline was greater for people without health insurance compared with those with health insurance (2.3% compared with 1.9%). Among persons who currently had asthma, there was a significant decline in the use of antibiotics and an absolute percentage change of 2.6%. There was no change in use for those who currently had chronic bronchitis and/or ever had emphysema.

Among the categories of antibiotics examined, there were significant declines in the use of penicillins, cephalosporins and macrolide derivatives (Table 2). The absolute percentage changes between 1999–2002 and 2011–12 for the three categories were 1.0%, 0.4% and 0.3%, respectively. Within the time periods examined, there was a significant decline in the

use of penicillins and macrolide derivatives between 2003–06 and 2007–10. Among the three individual antibiotics examined, only the use of amoxicillin declined significantly.

Discussion

The CDC has identified antibiotic resistance as a top public health concern and has promoted adherence to appropriate prescribing guidelines since the mid-1990s. This study, along with others that have examined trends in the dispensing of antibiotics, can provide valuable information on antibiotic use in the USA.

From 1999–2002 to 2011–12, when the CDC programmes were active and when the pneumococcal conjugative vaccines PCV7 and PCV13 became available (2000 and 2010, respectively),⁷ there was a significant decline in the use of antibiotics among the US population. The declines mirror those found in prior studies that have examined the dispensing of antibiotics since the mid-1990s.⁷ Within most population subgroups examined, data showed a significant decline in the percentage of persons who were using antibiotics. This decline was observed in most age groups, males and females, race/Hispanic origin groups, those with and without health insurance coverage and persons who currently had asthma.

Although the declines in overall antibiotic use were statistically significant, the magnitudes of the declines ranged from 1.2 to 6.8 percentage points, indicating that the decline in antibiotic use is not universal among all subpopulations. The largest decline occurred among children under the age of 2 years, where the percentage of antibiotic users declined almost by half. Antibiotic use among this group is of great interest due to their high use of antibiotics and because the CDC had focused on educating parents of young children about appropriate uses of antibiotics.

The assessment of categories of antibiotics and individual drugs revealed that the decline in the use of antibiotics was not concentrated among one category of antibiotics. Significant declines were reported for three categories (penicillins, cephalosporins and macrolide derivatives). Among individual antibiotics, there was a significant decline in the use of amoxicillin, which mirrors findings from studies of their use in ambulatory settings.

This study has several limitations. First, we cannot determine whether the decline in the use of antibiotics was for appropriate or inappropriate uses. Due to the relatively small number of persons taking some of the categories of antibiotics, some of the CIs were wide and may have resulted in a lack of power to identify significant covariate effects and linear trends. Caution should be exercised when conducting inference for prevalence estimates based on small numbers of outcomes or means based on small sample sizes. Our prevalence rate is based on use within the past 30 days and variation may exist between this study and others that examined antibiotic use using different time periods (i.e. past week and past 2 weeks). In addition, due to most regimens of antibiotics lasting 10–14 days, respondents may have used them within the past 30 days, but could have forgotten they took them or discarded their containers. Thus, the prevalence rates reported may be a conservative estimate of

antibiotic use. Finally, we cannot determine which factors were responsible for the decline in antibiotic use during the time periods examined.

The strengths of this study are that the data come from a large, nationally representative sample of the US population, that the data include detailed demographic and health information, which allowed us to assess use of antibiotics across several population subgroups, and that we were able to examine trends in the use of categories of antibiotics and also individual antibiotics. In addition, data on prescription medication use come primarily from observing respondents' medication containers (not self-report) and include antibiotics prescribed across multiple healthcare settings.

This study revealed that there has been a significant decline in the use of antibiotics among the US non-institutionalized population during the past 13 years. This decline was found among numerous population subgroups of interest (e.g. children under the age of 2 years and people with asthma), but for some subpopulations no decline was found. Declines were also observed among different categories of antibiotics. Due to concerns about the threat of antimicrobial resistance, it is important to continue monitoring the use of antibiotics.

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Disclaimer

The findings and conclusions in this article are those of the authors and not necessarily those of the CDC.

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Table 1. Use of prescription antibiotics^a in the past 30 days among US children and adults, NHANES 1999–2012

	1999–2002		2003–06		2007–10		2011–12		P value for overall linear Trend ^b	Absolute percentage change (1999–2002 versus 2011–12)
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)		
Overall	20814	6.1 (5.4–6.8)	20347	5.6 (5.0–6.3)	20577	4.2 (3.8–4.7)**	9706	4.1 (3.6–4.6)	<0.001	2.0
Age groups (years)										
0–1	1635	15.5 (12.9–18.7)	1690	10.9 (9.0–13.1)*	1532	11.7 (9.5–14.5)	620	8.7 (6.7–11.2)	0.001	6.8
2–5	1801	9.1 (7.2–11.4)	1975	7.3 (5.3–10.0)	1893	7.1 (5.4–9.4)	973	6.6 (3.3–12.6) ^f	0.34	2.5
6–11	2345	6.1 (4.3–8.6)	2176	5.8 (4.3–7.9)	2510	4.8 (3.6–6.3)	1325	2.7 (1.5–4.8)***	0.01	3.4
12–17	3722	8.0 (6.5–9.9)	3412	7.8 (6.5–9.3)	1971	4.8 (3.4–6.7)**	968	5.1 (2.8–9.3)	0.05	2.9
18–39	4736	6.0 (4.9–7.3)	4797	5.4 (4.4–6.6)	4576	4.5 (3.7–5.5)	2250	4.7 (3.9–5.8)	0.04	1.3
40–59	2934	5.0 (3.9–6.3)	2865	4.8 (4.1–5.7)	3906	3.0 (2.5–3.6)**	1801	3.0 (2.0–4.5)	0.01	2.0
60	3641	4.3 (3.5–5.1)	3432	4.4 (3.8–5.1)	4189	3.1 (2.5–3.9)**	1769	3.5 (2.4–5.0)	0.11	0.8
Sex										
male	10144	5.6 (4.8–6.6)	9989	4.5 (3.9–5.3)	10268	4.0 (3.5–4.6)	4831	3.2 (2.5–4.1)	<0.001	2.4
female	10670	6.5 (5.8–7.2)	10358	6.6 (5.8–7.4)	10309	4.4 (3.9–5.0)**	4875	4.9 (4.0–5.9)	<0.001	1.6
Race/Hispanic origin ^{c,d}										
non-Hispanic white	7909	6.9 (5.9–8.0)	8014	6.2 (5.5–7.0)	8489	4.9 (4.3–5.5)**	2964	4.9 (4.0–5.9)	<0.001	2.0
non-Hispanic black	4853	4.4 (3.7–5.2)	5321	4.3 (3.4–5.4)	4147	3.7 (3.2–4.4)	2667	3.2 (2.6–4.0)	0.02	1.2
Mexican American	6126	3.9 (3.4–4.6)	5352	3.9 (3.2–4.7)	4519	3.2 (2.5–4.1)	1345	3.8 (2.7–5.4)	0.23	0.1
Health insurance status										
no insurance	3915	4.4 (3.2–6.1)	3610	3.6 (2.7–4.7)	3989	2.9 (2.3–3.7)	1692	2.1 (1.5–3.1)	0.003	2.3
have insurance	16524	6.4 (5.7–7.3)	16564	6.0 (5.3–6.7)	16555	4.5 (4.0–5.1)**	7995	4.5 (3.8–5.2)	<0.001	1.9
Respiratory conditions										
asthma ^e	784	7.8 (5.6–10.9)	1709	9.0 (6.9–11.6)	1698	5.7 (4.4–7.4)**	877	5.2 (3.5–7.8)	0.02	2.6
chronic bronchitis and/or emphysema ^{f,g}	417	7.9 (5.0–12.2)	443	10.4 (7.3–14.7)	555	6.6 (4.5–9.7)	204	6.3 (3.8–10.1)	0.28	1.6

Interview sample weights were utilized to adjust for differential probabilities of selection and the complex sampling design.

Respondents were asked: 'In the past 30 days, have you used or taken medication for which a prescription is needed?'

^aTopical antibiotics are excluded from this analysis.

^bTest for an overall linear trend using Stata's 'contrast' command.

^cAge-adjusted to the 2000 US Census population using age groups 0–1 year, 2–5 years, 6–11 years, 12–17 years, 18–39 years, 40–59 years and 60 years.

^dEstimates for persons of other race/ethnicity groups are not provided separately, but members of this group are included in total estimates.

^eCurrently have asthma. Question restricted to respondents aged 1 year. Data available from 2001 to 2012.

^fCurrently have chronic bronchitis. Question restricted to respondents aged 20 years. Data available from 1999 to 2012.

^gEver had emphysema. Question restricted to respondents aged 20 years. Data available from 1999 to 2012.

* Statistically significant differences between 1999–2002 and 2003–06 estimates ($P < 0.05$).

** Statistically significant differences between 2003–06 and 2007–10 estimates ($P < 0.05$).

*** Statistically significant differences between 2007–10 and 2011–12 estimates ($P < 0.05$).

!Estimate does not meet standard of statistical reliability and precision (relative standard error $> 30\%$ and $< 40\%$).

Table 2.

Use of antibiotics by category and individual antibiotics in the past 30 days among US children and adults, NHANES 1999–2012 ^a

	1999–2002		2003–06		2007–10		2011–12		P value for overall linear trend ^b	Absolute percentage change (1999–2002 versus 2011–12)
<i>n</i>	% (95% CI)	<i>n</i>	% (95% CI)	<i>n</i>	% (95% CI)	<i>n</i>	% (95% CI)			
Antibiotic categories ^c	20814		20347		20577		9706			
penicillins	2.7 (2.3–3.2)		2.3 (1.9–2.7)		1.6 (1.4–1.8)**		1.7 (1.3–2.2)		<0.001	1.0
cephalosporins	0.9 (0.7–1.1)		0.7 (0.6–0.9)		0.6 (0.4–0.8)		0.5 (0.3–0.8)		0.02	0.4
macrolide derivatives	0.8 (0.6–1.1)		0.9 (0.7–1.1)		0.5 (0.4–0.6)**		0.5 (0.3–0.8)		0.01	0.3
tetracyclines	0.7 (0.6–0.9)		0.7 (0.5–0.9)		0.7 (0.5–0.9)		0.7 (0.5–1.1)		0.99	0.0
sulphonamides	0.4 (0.3–0.5)		0.4 (0.2–0.5)		0.4 (0.3–0.5)		0.3 (0.2–0.5)		0.44	0.1
quinolones	0.4 (0.3–0.5)		0.5 (0.4–0.7)		0.4 (0.3–0.6)		0.3 (0.2–0.6)		0.58	0.1
urinary anti-infectives	0.2 (0.2–0.3)		0.3 (0.2–0.4)		0.2 (0.1–0.3)		0.2 (0.2–0.4)		0.78	0.0
lincomycin derivatives	0.1 (0.1–0.2)		0.2 (0.1–0.3)		0.1 (0.1–0.2)		0.1 (0.1–0.3) ^f		0.86	0.0
miscellaneous antibiotics ^d	0.2 (0.1–0.3)		0.2 (0.1–0.3)		0.1 (0.04–0.1)**		0.2 (0.01–0.04) ^g		0.55	0.0
Individual antibiotics										
amoxicillin ^e	2.3 (1.9–2.8)		1.9 (1.5–2.3)		1.3 (1.1–1.6)**		1.4 (1.1–1.9)		0.001	0.9
cefalexin	0.5 (0.4–0.7)		0.4 (0.3–0.5)		0.4 (0.3–0.5)		0.4 (0.2–0.7) ^h		0.22	0.1
azithromycin	0.3 (0.2–0.5)		0.5 (0.4–0.6)		0.4 (0.3–0.5)		0.5 (0.3–0.8)		0.54	0.2

Interview sample weights were utilized to adjust for differential probabilities of selection and the complex sampling design. Respondents were asked: ‘In the past 30 days, have you used or taken medication for which a prescription is needed?’

^aTopical antibiotics are excluded from this analysis.

^bTest for an overall linear trend using Stata’s ‘contrast’ command.

^cLevel 2 drug categories from the Multum Lexicon Drug Database. Glycopeptide antibiotics are not shown due to only three respondents indicating that they used them.

^dAntibiotics in this category include chloramphenicol and metronidazole.

^eIncludes multi-ingredient drugs that contain amoxicillin.

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* Statistically significant differences between 1999–2002 and 2003–06 estimates ($P < 0.05$).

** Statistically significant differences between 2003–06 and 2007–10 estimates ($P < 0.05$).

*** Statistically significant differences between 2007–10 and 2011–12 estimates ($P < 0.05$).

! Estimate does not meet standard of statistical reliability and precision (relative standard error $> 30\%$ and $< 40\%$).

!! Estimate does not meet standard of statistical reliability and precision (relative standard error $> 40\%$ and $< 50\%$).