ORIGINAL ARTICLE

Monthly trends in antimicrobial consumption and influenza incidence at the community level in 2014 in Poland

Anna Olczak-Pieńkowska, Anna Skoczyńska, Waleria Hryniewicz

Department of Epidemiology and Clinical Microbiology, National Medicines Institute, Warsaw, Poland

KEY WORDS

antibiotic resistance, community level, influenza incidence, seasonal antimicrobial consumption

ABSTRACT

INTRODUCTION Antibiotic resistance is nowadays one of the most important public health threats. It is mainly caused by inappropriate antibiotic usage.

OBJECTIVES We aimed to characterize the seasonal trends of antimicrobial consumption (AC) and to assess the possible relation between AC and the incidence of influenza at the community level in 2014 in Poland.

PATIENTS AND METHODS Influenza incidence, AC, and the number of inhabitants vaccinated against influenza were examined at the community level. The AC was assessed on the basis of sales data and then converted to defined daily doses (DDDs) per 1000 inhabitants per day according to the Anatomical Therapeutic Chemical Classification System and the DDD methodology. The data on the incidence of influenza and influenza-like cases were based on notifications from primary care doctors.

RESULTS The majority of antimicrobials were consumed at the community level. The mean community consumption of antibacterials for systemic use in Poland in 2014 was 22.50 DDDs per 1000 inhabitants per day. The most frequently consumed substances were oral amoxicillin, amoxicillin and enzyme inhibitor, and cefuroxime. Two seasonal peaks of AC were observed. Seasonal trends in AC were similar to trends in influenza incidence. The highest AC was observed in a voivodeship with the highest influenza incidence.

CONCLUSIONS The extent of outpatient AC and the seasonal coincidence of influenza and AC pose an important risk for antibiotic overuse and misuse, which are the main causes of antibiotic resistance.

INTRODUCTION

Antibiotic resistance is currently one of the top global health concerns.[1-5] There are several reasons for this phenomenon, but the main driving factors are the overuse and misuse of antimicrobials.[6,7] It was shown that the higher the antimicrobial consumption (AC), the higher the proportion of resistant pathogens.[8,9] A striking example of antibiotic misuse at the community level, a phenomenon contributing to emergence and spread of antibiotic resistance, is the high prescription rate of antibiotics for respiratory tract infections (RTIs), caused mainly by viruses.[10-12] The lack of knowledge that antibiotics do not act on viruses may result in inappropriate antibiotic use.[13,14] The strategies to prevent development and dissemination of antimicrobial resistance are complex and require a multidisciplinary approach.[7,8] The surveillance of antimicrobial usage reveals areas of overuse and misuse and helps identify vulnerable regions, sectors, and seasons. This facilitates the planning of interventions aimed at antibiotic resistance control.

The aim of this study was to characterize seasonal trends in AC in 2014 at the community level in Poland and to assess the possible relation between the AC and incidence of influenza.

PATIENTS AND METHODS

This study focused on the community (outpatient) sector, although total and hospital consumption levels were also calculated to indicate the overall AC in Poland. Data on AC were provided through the courtesy of Quintiles IMS, a company monitoring the pharmaceutical

Correspondence to:
Anna Olczak-Pieńkowska, MPH, Department of Epidemiology and Clinical Microbiology, National Medicines Institute, ul. Chełmska 30/34, 00-725 Warsaw, Poland, phone: +48 22 841 33 67, email: a.olczak@nil.gov.pl
Received: September 7, 2018.
Revision accepted: October 29, 2018.
Published online: November 7, 2018.
Conflict of interest: none declared.
Pol Arch Intern Med. 2018; 128 (12): 731-738
doi:10.20452/pamw.4368

TABLE 1 Antibiotics with the highest consumption at the community level in 2014 in Poland

Antibiotic[a]	Annual consumption (defined as daily doses per 1000 inhabitants per day)	Community consumption out of total consumption, %	Included in national recommendations?[b]
Amoxicillin	4.839	21.51	Yes
Amoxicillin and enzyme inhibitor	3.735	16.60	Yes
Cefuroxime	2.076	9.23	Yes
Doxycycline	1.858	8.26	Yes
Clarithromycin	1.429	6.35	Yes
Azithromycin	1.249	5.55	Yes
Ciprofloxacin	0.712	3.16	No
Sulfamethoxazole and trimethoprim	0.468	2.08	No
Phenoxymethylpenicillin	0.211	0.94	Yes
Levofloxacin	0.154	0.69	Yes
Total consumption	22.503	100.00	–

a Antibacterials for systemic use (code J01 in the Anatomical Therapeutic Chemical Classification System). All antibiotics were administered orally.

b National recommendations for community-acquired respiratory tract infections.[16]

Abbreviations: J01, antibacterials for systemic use

market. The data were based on retail sales at the pharmacy level (assumed to reflect community consumption) and on wholesaler sales to hospitals (hospital consumption).

The data on the numbers and contents of packages were used in calculations to express AC in defined daily doses (DDDs) according to the methodology proposed by the World Health Organization Collaborating Centre for Drug Statistics Methodology.[15] In the calculations of consumption trends for specific months, a variable number of days was considered. We focused on the following antimicrobials or their groups: antibacterials for systemic use (J01 code in the Anatomical Therapeutic Chemical [ATC] Classification System); antibacterials for systemic use listed in national recommendations (approved by the Polish Ministry of Health) as the main treatment options for community-acquired RTIs (r-CA-RTI group; TABLE 1)[16]; and oseltamivir (neuraminidase inhibitor), an antiviral for influenza treatment (antivirals for systemic use, ATC code J05).

The data on the incidence of influenza and influenza-like cases by month and voivodeship were obtained from the database of the National Institute of Public Health–National Institute of Hygiene (NIPH-NIH). The weekly NIPH-NIH epidemiological reports contain information on the numbers of influenza-related cases, suspicions, and deaths. For the purpose of infectious diseases surveillance in European Union countries, the NIPH-NIH reports define influenza as cases with a clinical or laboratory diagnosis of influenza, together with all clinically diagnosed influenza-like cases and RTIs fulfilling the criteria for the definition of influenza.[17] As the reports were based on notifications from primary care doctors, the data on influenza incidence were considered as community-level data.

The NIPH-NIH reports were also the source of data on the number of inhabitants vaccinated against influenza per voivodeship. These data were expressed as the number of individuals vaccinated per 1000 inhabitants per day (VID).

Demographic data on the number of inhabitants by month and voivodeship were obtained from the Central Statistical Office of Poland (Główny Urząd Statystyczny [GUS]). The number of inhabitants is estimated by GUS on a quarterly basis and provided for the last day of the quarter. For the purpose of this analysis, it was assumed that the population size was stable during each of the 3 months that constituted a quarter. The GUS methodology calculates the number and structure of the population on the basis of the most recent population and housing census.[18]

AC levels were expressed as DDDs. Mean values for AC levels and influenza incidence by month and voivodeship were calculated. AC levels and influenza incidence were also described using range and standard deviation (SD). The coefficient of variation was calculated to show variability in the mean AC levels and influenza incidence by month and voivodeship. Voivodeships were ranked according to AC levels and influenza incidence. Trends were assessed to show changes in AC and influenza incidence over time. Finally, the coefficient of determination was used to assess the correlation between AC and influenza incidence.

RESULTS The consumption of antibacterials for systemic use at the community level in Poland in 2014 was 22.50 DDDs per 1000 inhabitants per day (DID) and represented 94.08% of the total consumption of antibacterials. During the study, consumption at the community level ranged from 15.04 DID to 27.31 DID (SD, 3.72). Two seasonal peaks in consumption

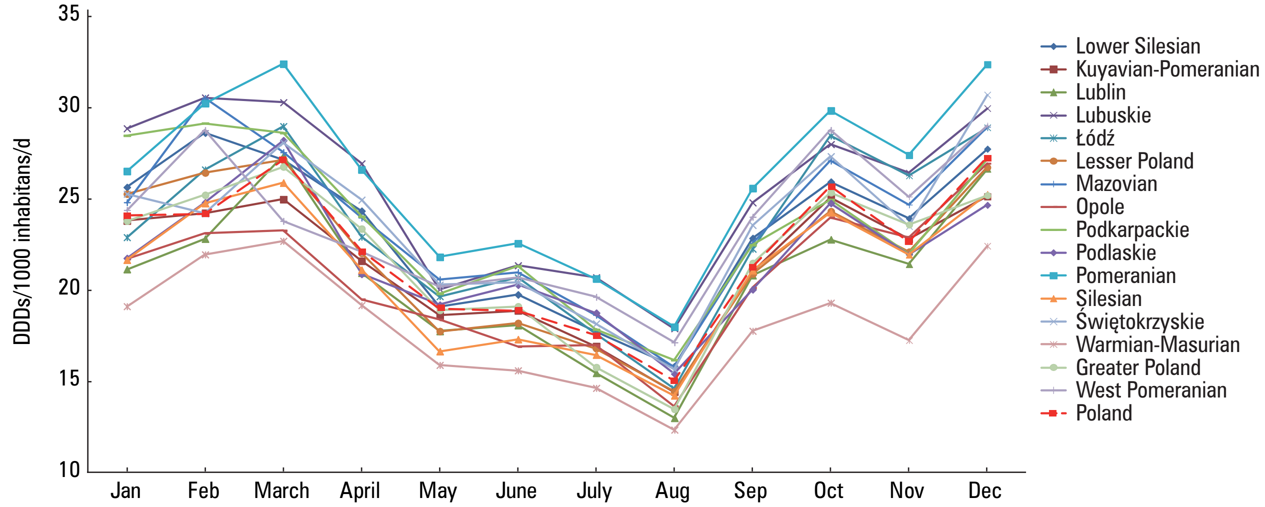

FIGURE 1 Consumption of antibacterials for systemic use (Anatomical Therapeutic Chemical Classification System code J01) in 2014 by voivodeship in Poland. Data were expressed as defined daily doses (DDDs) per 1000 inhabitants per day.

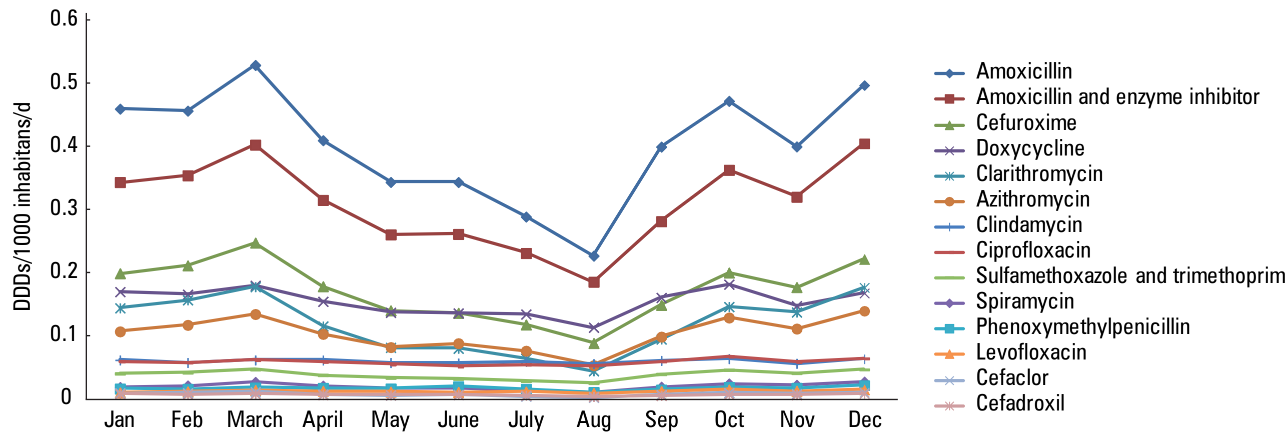

FIGURE 2 Antibiotics with the highest consumption at the community level in 2014 in Poland. All antibiotics were administered orally. Data were expressed as defined daily doses (DDDs) per 1000 inhabitants per day.

were observed: in February–March and October–December. Although the consumption levels differed between voivodeships, the overall trends were similar. Consumption was consistently the lowest in Warmian-Masurian Voivodeship and the highest in Pomeranian Voivodeship. The coefficient of variation was 16.83% (FIGURE 1).

The consumption at the community level of the 15 most common antibacterials (out of all 57 antibacterials used) reached 17.73 DID (79.81% of the total community consumption). The most common substances were oral amoxicillin, oral amoxicillin and enzyme inhibitor, and oral cefuroxime (all with indications for RTIs) (TABLE 1). Consumption trends for the most common substances were stable throughout the studied period except doxycycline, for which the trend did not show characteristic peaks (FIGURE 2).

The r-CA-RTI group was selected for a broader analysis and included the 10 most common antibiotics used for outpatient oral treatment of RTIs. Most of the r-CA-RTI consumption (97.47%) occurred in the community sector and constituted 67.64% of the total consumption of antibacterials at the community level. All of the analyzed r-CA-RTI substances were included in the group of the most frequently consumed antibacterials for systemic use in the community sector (TABLE 1). The same consumption peaks were observed for the r-CA-RTI group as for the overall J01 group. The mean monthly consumption level of r-CA-RTI was 15.29 DID, ranging from 8.74 DID in August to 19.62 DID in March (SD, 3.29) (FIGURE 3).

The coefficient of variation for r-CA-RTI consumption was 21.56%. Consumption levels of r-CA-RTI per voivodeship were similar to those for the whole J01 group, with the highest consumption observed for Pomeranian Voivodeship and the lowest—for Warmian-Masurian Voivodeship.

Because of the resistance patterns of the influenza virus in 2014 in Poland, oseltamivir was recommended as an antiviral drug. The consumption

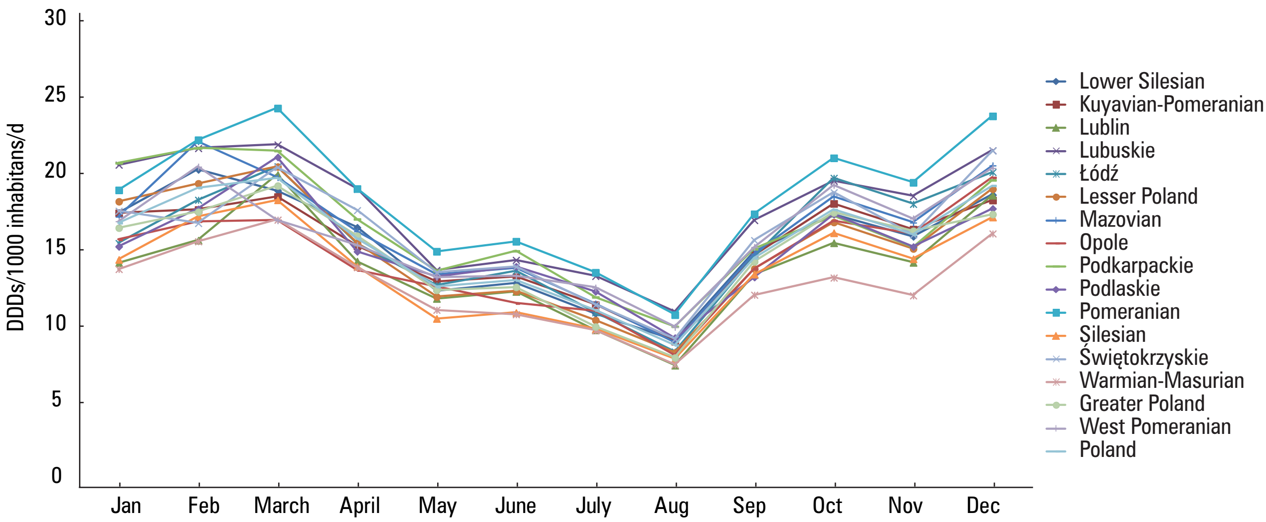

FIGURE 3 Consumption of selected antibacterials for systemic use (Anatomical Therapeutic Chemical Classification System code J01) recommended for community-acquired respiratory tract infections. Data were expressed as defined daily doses (DDDs) per 1000 inhabitants per day and presented according to Polish voivodeships in 2014

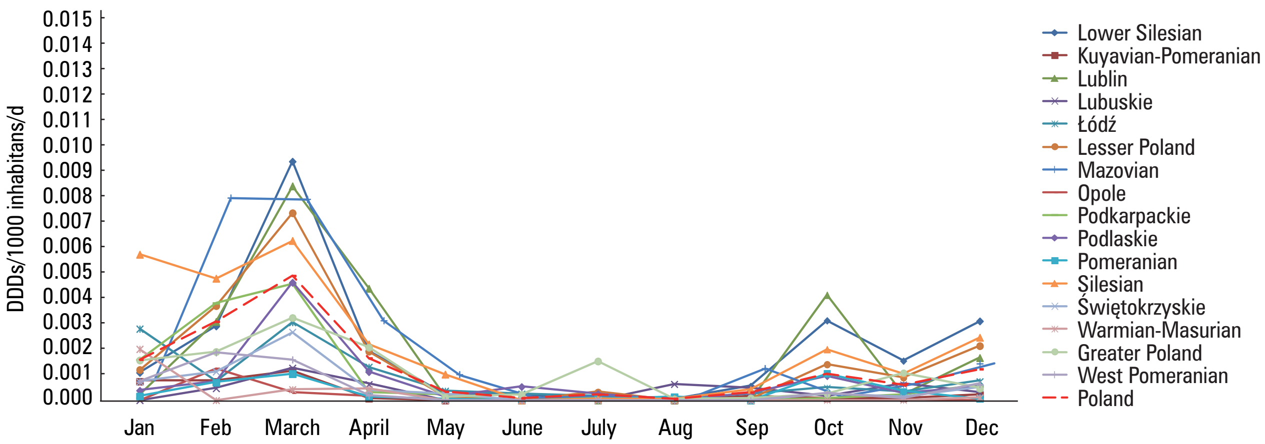

FIGURE 4 Consumption of oseltamivir at the community level by month and voivodeship in 2014 in Poland. Data were expressed as defined daily doses (DDDs) per 1000 inhabitants per day.

of oseltamivir at the community level in 2014 was 0.0013 DID (73% of the overall oseltamivir consumption). The monthly consumption ranged from 0.00005 DID in March to 0.00489 DID in August (SD, 0.0014), and the coefficient of variation was 1.09 (FIGURE 4). The consumption peak in March was about 5 times higher than that in October.

The incidence trends for influenza in 2014 showed seasonal peaks in February–March and October–December, with the lowest level in August. Similar trends were observed in different voivodeships. The highest influenza incidence was observed in Pomeranian Voivodeship and the lowest—in Warmian-Masurian Voivodeship. The incidence levels of influenza by month and voivodeship were stable, with trend curves almost parallel (FIGURE 5). In March, the influenza incidence level in Podlaskie Voivodeship was higher than the mean country level, while in Łódzkie Voivodeship, the incidence level reached the mean country level. In Pomorskie Voivodeship, the October peak for influenza incidence was significantly higher compared with other voivodeships (FIGURE 5).

The number of individuals vaccinated against influenza was calculated for 2013 and 2014. This is because the influenza season starts in autumn, and the study population may have also been vaccinated in 2013. As the data on the monthly number of vaccinated individuals were not available, we checked data from 2013 as a control for the number of vaccinated individuals. The comparison confirmed that the numbers were stable thus the vaccinated population in 2013/2014 was comparable.

The number of vaccinated individuals per 1000 VID was 24.12 in 2013 and 22.22 in 2014. In both years, the voivodeships with the lowest VID were: Pomeranian (18.61 in 2013 and 15.95 in 2014), Podkarpackie (19.43 in 2013 and 16.10 in 2014), and Lublin (20.07 in 2013 and 19.03 in 2014). The voivodeships with the highest VID were: West Pomeranian (31.66 in 2013 and 29.49 in 2014), Mazovian (31.29 and 28.25),

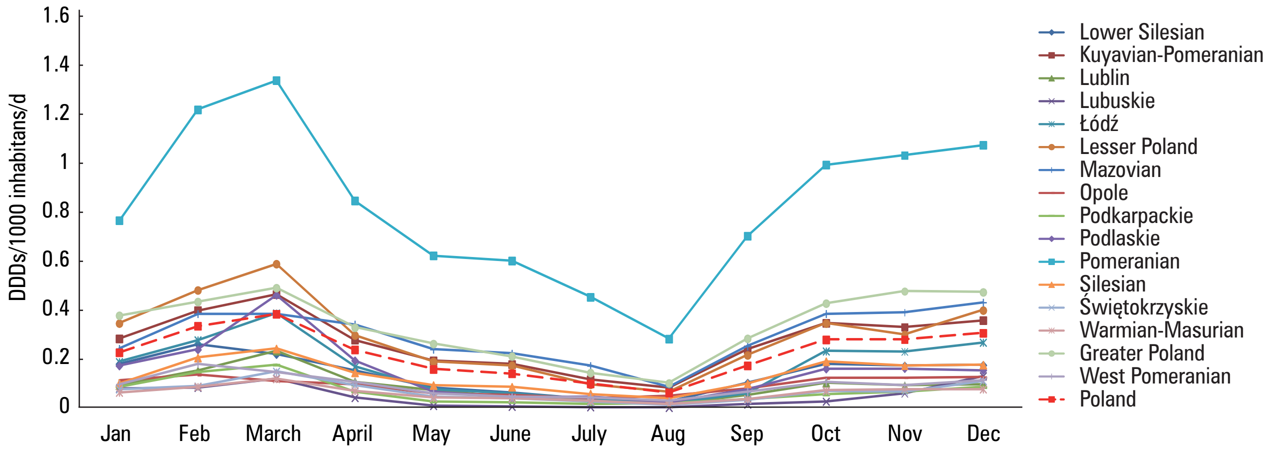

FIGURE 5 Influenza incidence by month and voivodeship in 2014 in Poland (influenza cases per 1000 inhabitants per day; red dashed line shows mean country incidence). Data were expressed as defined daily doses (DDDs) per 1000 inhabitants per day.

Lower Silesian (27.26 and 24.27), and Warmian-Masurian (25.66 and 25.60). The voivodeships with the highest and lowest VID differed almost by a factor of 2 (in 2014: 15.95 in Pomeranian Voivodeship vs 29.49 in West Pomeranian Voivodeship). The overall VID for Poland declined from 2013 to 2014 by 1.90. The decline was also observed in individual voivodeships (mean difference, 1.74 VID). The VID in specific voivodeships in 2014 was similar to the control year of 2013.

The influenza incidence trends were similar to the consumption trends observed for J01 and r-CA-RTI groups and showed similar seasonal peaks. The coefficient of variation for monthly influenza incidence was higher than for J01 and r-CA-RTI consumption and reached 42.32%.

The influenza incidence pattern by voivodeships in 2014 was more stable than the antibacterial consumption pattern.

Our analysis showed that Pomeranian Voivodeship, which showed the highest influenza incidence rate, also had the highest antibacterial consumption levels throughout most of 2014. Similarly, the voivodeship with the lowest antibacterial consumption (Warmian-Masurian) reported also one of the lowest influenza incidence level. The community consumption and influenza incidence rankings were similar. Pomeranian Voivedeship, as the voivodeship with the highest influenza incidence and antibacterial consumption, showed the lowest number of vaccinated inhabitants (both in 2013 and 2014). Consumption of the overall J01 group at the community level and the incidence levels of influenza markedly differed in specific months in 2014 in Lubuskie, Świętokrzyskie, and West Pomeranian Voivodeships (where the consumption was one of the highest, while influenza incidence one of the lowest). In addition, in Greater Poland and Kuyavian-Pomeranian Voivodeships, antibacterial consumption was lower than the mean country level but the influenza incidence was one of the highest.

The coefficient of determination showed the strongest correlation between influenza incidence and r-CA-RTI consumption ($R^2 = 0.9362$). A weaker correlation was observed for antibacterial consumption ($R^2 = 0.8738$), and the weakest correlation, for oseltamivir consumption ($R^2 = 0.6598$).

DISCUSSION This study reported for the first time annual trends for antibiotic and antiviral consumption due to influenza in Poland combined with data on influenza incidence and the number of inhabitants vaccinated against influenza.

The time frame (a calendar year) was selected to observe monthly trends in AC. We chose 2014 because it was the first year for which data on the total (hospital and community) consumption in Poland were available, providing a complete picture of AC distribution. Another reason for selecting 2014 was the availability of data on the number of vaccinated inhabitants. Moreover, the analysis of annual trends in influenza incidence and AC was justified by the fact that the dominant influenza virus in Poland in the 2013/2014 and 2014/2015 seasons was the same (AH1N1).[19,20]

In 2014, the average AC at the community level in 31 European reporting countries was 91.59% of the total consumption (range, 84.85%–94.67%). Our study showed that in 2014 in Poland, 94.08% of antimicrobials were consumed at the community level. Poland was among the top 10 European countries with the highest AC at the community level. This trend was maintained throughout the years 1998 and 2015 when the average annual outpatient level of AC exceeded the average European level.[21,22]

Our study also showed the highest consumption level for antibiotics belonging to the so called r-CA-RTI group (more than half of the total J01 consumption). The antibiotics with the highest consumption level in the community sector had at least one indication for use in RTI in their summary of product characteristics. The main contribution of antibiotics used in RTIs to AC was confirmed by a cross-national study analyzing data for the period from 1997 to 2002.[23] RTIs as the main indication for prescribing antibiotics in primary care settings were also mentioned in a comparative study of outpatient systemic antibacterial use in 2004 in the United States and 27 European countries.[24] An analysis of antibiotics prescribed in the years 2010 to 2011 in the United States showed that approximately 50% of acute respiratory conditions led to inappropriate antibiotic prescriptions.[25] Similar conclusions were reported by another American study that evaluated adult upper RTIs in outpatient settings from 1998 to 2003,[26] by a review of antibiotic use for acute RTIs,[27] and by a survey assessing data on the patterns of ambulatory antibiotic prescription in adults in the years from 2007 to 2009.[28]

Our results suggest that r-CA-RTI antibiotics should be carefully monitored to minimize the risk of their misuse and overuse, which is consistent with a report by Molstad et al.[29] An example of an effective prevention program against antibiotic resistance is the strategy implemented in Sweden. During 20 years of this program, a significant reduction in antibiotic prescription rates for RTIs, especially in children, was achieved with appropriate educational activities and surveillance of antibiotic resistance and consumption.[29]

Our analysis of the seasonal trends of AC and its possible correlation with the influenza incidence highlights a few important issues. We observed that the seasonal peaks in the consumption of antibacterials for systemic use during the year corresponded to the peaks in influenza incidence and that the seasonal peaks in influenza incidence preceded the peaks in antibacterial consumption at the community level. An escalation in antibiotic use during or after influenza peaks may result from an epidemic wave and a rising incidence of bacterial coinfections or bacterial infections secondary to influenza infections. Nevertheless, it is difficult to conclude if antibiotic prescriptions in the community setting in Poland were based on the precise identification of the etiology of infections. There are no data linking AC to diagnosis.

Within the J01 therapeutic group, the consumption trends were similar between the most frequently used substances. The only exception was doxycycline: its consumption trend did not show the characteristic fall in August or peaks in March and October. This might be explained by increased rates of doxycycline prescriptions for borreliosis, which occurs with high incidence during the summer months in Poland.[30]

We also found that the trends for influenza incidence and AC at the community level were parallel. However, the peak r-CA-RTI consumption during the study occurred earlier than the peak J01 consumption. In comparison with the J01 therapeutic group, the consumption trend for r-CA-RTI was more consistent with the trend observed for influenza incidence. Another Polish analysis showed that the peak of the laboratory-confirmed influenza-like virus detection preceded the peak of the influenza virus detection.[20] These observations suggest a relationship between the incidence of viral RTIs and r-CA-RTI overuse. Antibiotic misuse in viral RTIs during influenza periods were confirmed by several studies. Nitsch-Osuch et al[31] described the overuse of antibiotics and underuse of antivirals in children with influenza in Poland. Among the most frequently administered antibiotics, the authors listed amoxicillin with clavulanic acid, cefuroxime, and amoxicillin—the same 3 most commonly used antibiotics as reported in our study. Several studies conducted in the United States showed similar correlations. One of them revealed a substantial proportion of antibiotics prescribed to children diagnosed with respiratory disorders that typically are not cured by antibiotics (like common cold, otitis media, and acute bronchitis).[32] Another study reported that over one-third of ambulatory visits with a diagnosis of influenza resulted in prescription of an antibiotic.[33] The above studies emphasize that incorrect prescription of antibiotics to treat mostly viral respiratory infections may be harmful and promotes the emergence and spread of antibiotic resistance.

The seasonality of influenza incidence is a complex issue. Factors such as air temperature or seasonal cooling of the nasal airways that compromise the local respiratory defense were described to be correlated with respiratory diseases.[34] Cycles in host resistance to infection (immune response), variations in the survival of the virus (ambient temperature, humidity, vapor pressure), and factors connected with crowding were also indicated among the causes of influenza seasonality.[35] It was also concluded that the seasonality of nonpandemic influenza is conditioned not only by singular factors but also by their interaction and complexity.[36]

With respect to oseltamivir consumption trends, our study revealed an evident peak at the beginning of 2014. As our analysis was based on sales data, this observation might suggest oseltamivir stockpiling (at personal and health care facility levels). In a review of systemic antiviral use in Europe published in 2011, antiviral stockpiles were described to be provided to primary health care professionals for distribution without prescription during the outbreak of the AH1N1 pandemic in 2009 in Belgium. The same study reported stockpiles of oseltamivir purchased in 2005 during the avian flu pandemic in several European countries.[30] Another study described that the peak of oseltamivir use in European countries occurred mostly during the first quarter of the year. This might reflect a stronger correlation of the peak oseltamivir use with the perceived threat of a potential influenza pandemic, stimulated by the media, as compared with real influenza incidence.[37] Similar reasons for stockpiling were also reported in Norway[38] and in the United States.[39]

We also explored influenza vaccination as a tool for reducing influenza incidence and the resulting AC. We found voivodeships with the highest AC and influenza incidence levels and the lowest number of vaccinated inhabitants. Variations between voivodeships in the number of inhabitants vaccinated against influenza, AC, and influenza incidence levels indicate a potential need for interventions. The correlation between influenza vaccination and AC was also reported in other studies. It was concluded that the misuse of antibiotics for influenza treatment can be limited by reducing the viral spread by vaccination and other preventive measures such as hand hygiene, rapid point-of-care influenza tests, rational use of antivirals, or education of physicians and parents regarding the appropriate use of antibiotics.[39] The measures to lower excessive antibiotic prescription during influenza periods was also described in the Netherlands.[40]

We are aware that using sales data as the basis for the analysis of AC may not exactly reflect the medications consumed, which might be considered a study limitation. Still, the data used in this study were the most comprehensive among the data available in Poland and covered the whole population. A more specific assessment of the extent to which prescribed treatments comply with national recommendations would require monitoring of the exact consumed values, and this would be possible only at the patient level in a sampled study.

Our study would have a greater value if we had included data on the etiology of infections for which antibiotics were prescribed. A study by Low[38] showed that the AC was twice the level justified by etiology.[38] Unfortunately, these data are not available in Poland, so further studies are needed to investigate this issue.

Conclusions AC occurs mostly at the community level. Therefore, the surveillance of consumption and measures to improve antibiotic use need to be enhanced, particularly in the outpatient sector. The extent of AC at the community level and the seasonal correlation of influenza incidence with AC pose an important risk for antibiotic overuse and misuse, which are the main reasons for the spread of antibiotic resistance. Data on regional differences in AC derived from epidemiological surveillance programs should be considered in developing interventions aimed both at infection control (eg, vaccination) and at rational antibiotic policy. Infection control measures and reasonable prescription practices should be promoted and implemented with special attention to specific geographic regions and months of the highest AC and influenza incidence levels as well as the areas with the lowest number of inhabitants vaccinated against influenza.

ACKNOWLEDGMENTS This study was supported by the National Programme for Protection of Antibiotics (NPOA) funded by the Ministry of Health. We would like to thank Maya Czeneszew and Zdzisław Markiewicz for English language editing and QuintilesIMS Poland for providing access to antimicrobial consumption database.

CONTRIBUTION STATEMENT All authors contributed to the design of the research. AOP collected and analyzed the data. All authors edited and approved the final version of the manuscript.

REFERENCES

1 World Health Organization. Antimicrobial resistance: global report on surveillance. World Health Organization website. https://www.who.int/drugresistance/documents/surveillancereport/en/. Published 2014. Accessed November 22, 2018.

2 The review on antimicrobial resistance. Tackling drug-resistant infections globally: final report and recommendations. https://amr-review.org. Published May 2016. Accessed November 22, 2018.

3 Ventola CL. The antibiotic resistance crisis, part 1: causes and threats. P T. 2015; 40: 277-283.

4 Laxminarayan R, Matsoso P, Pant S, et al. Access to effective antimicrobials: a worldwide challenge. Lancet. 2016; 387: 168-175.

5 Lawrence R, Jeyakumar E. Antimicrobial resistance: a cause for global concern. BMC Proc. 2013; 7 (suppl 3): 1-14.

6 Holmes AH, Moore LSP, Sundsfjord A, et al. Understanding the mechanisms and drivers of antimicrobial resistance. Lancet. 2016; 387: 176-187.

7 Davies J, Davies D. Origins and evolution of antibiotic resistance. Microbiol Mol Biol Rev. 2010; 74: 417-433.

8 Van de Sande-Bruinsma N, Grundmann H, Verloo D, et al. Antimicrobial drug use and resistance in Europe. Emerg Infect Dis. 2008; 14: 1722-1730.

9 Levy SB. Factors impacting on the problem of antibiotic resistance. J Antimicrob Chemother. 2002; 49: 25-30.

10 Gonzales R, Bartlett JG, Besser JG, et al. Principles of appropriate antibiotic use for treatment of nonspecific upper respiratory tract infections in adults: background. Ann Emerg Med. 2001; 37: 698-702.

11 Hinnerskov M, Therkildsen JM, Cordoba G, Bjerrum L. Macrolide overuse for treatment of respiratory tract infections in general practice. Dan Med Bull. 2011; 58: A4356.

12 Schwartz B, Bell DM, Hughes JM. Preventing the emergence of antimicrobial resistance: a call for actions by clinicians, public health officials and patients. JAMA. 1997; 278: 944-945.

13 Brooks L, Shaw A, Sharp D, et al. Towards a better understanding of patients' perspectives of antibiotic resistance and MRSA: a qualitative study. Fam Pract. 2008; 25: 341-348.

14 Costelloe C, Metcalfe C, Lovering A, et al. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. BMJ. 2010; 340: c2096.

15 WHO Collaborating Centre for Drug Statistics Methodology, Norwegian Institute of Public Health. International language for drug utilization research. www.whocc.no. Accessed November 22, 2018.

16 Hryniewicz W, Albrecht P, Radzikowski A, et al; Narodowy Program Ochrony Antybiotyków. Rekomendacje postępowania w pozaszpitalnych zakażeniach układu oddechowego. http://www.antybiotyki.edu.pl/pdf/Rekomendacje2016.pdf. Published 2016. Accessed November 22, 2018.

17 Department of Epidemiology and Surveillance of Infectious Diseases. Laboratory of Monitoring and Epidemiological Analysis. Influenza and influenza-like illness in Poland. National Institute of Public Health - National Institute of Hygiene website. http://wwwold.pzh.gov.pl/oldpage/epimeld/grypa/index.htm. Updated November 23, 2018. Accessed November 30, 2018.

18 Population by sex, feminization rate, population density. Statistics Poland website. http://swaid.stat.gov.pl/Demografia_dashboards/Raporty_predefiniowane/RAP_DBD_DEM_1.aspx. Accessed January 2018.

19 Kondratiuk K, Czarkowski M P, Hallmann-Szelińska E, et al. Influenza in Poland in 2013 and 2013/2014 epidemic season. Przegl Epidemiol. 2016; 70: 407-419.

20 Hallmann-Szelińska E, Rabczenko D, Bednarska K, et al. A comparative analysis of influenza virus infections in the 2013/2014 and 2014/2015 epidemic season in the reporting system, for different age groups in Poland. Family Medicine & Primary Care Review. 2016; 18: 244-249.

21 European Centre for Disease Prevention and Control. Summary of the latest data on antibiotic consumption in the European Union: ESAC-Net Surveillance data: 2016. https://ecdc.europa.eu/en/publications-data/summary-latest-data-antibiotic-consumption-eu-2016. Published November 2016. Accessed November 22, 2018.

22 European Centre for Disease Prevention and Control. Surveillance of antimicrobial consumption in Europe, 2010. Stockholm, Sweden: ECDC; 2013. https://ecdc.europa.eu/en/publications-data/surveillance-antimicrobial-consumption-europe-2010. Accessed November 22, 2018.

23 Goosens H, Ferech M, Coenen S, Stephens P; and the European Surveillance of Antimicrobial Consumption Project Group. Comparison of outpatient systemic antibacterial use in 2004 in the United States and 27 European Countries. Clin Infect Dis. 2007; 44: 1091-1095.

24 Goosens H, Ferech M, Stichele RV, Elseviers M. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. Lancet. 2005; 365: 579-587.

25 Fleming-Dutra KE, Hersh AL, Shapiro DJ. Prevalence of inappropriate antibiotic prescriptions among US ambulatory care visits, 2010-2011. JAMA. 2016; 315: 1864-1873.

26 Gill JM, Fleischut P, Haas S, et al. Use of antibiotics for adult upper respiratory infections in outpatient settings: a national ambulatory network study. Fam Med. 2006; 38: 349-354.

27 Harris AM, Hicks LA, Qaseem A. Appropriate antibiotic use for acute respiratory tract infections in adults: advice for high-value care from the American College of Physicians and the Centers for Disease Control and Prevention. Ann Intern Med. 2016; 164: 425-434.

28 Shapiro DJ, Hicks LA, Pavia AT, Hersh AL. Antibiotic prescribing for adults in ambulatory care in the USA, 2007-09. J Antimicrob Chemother. 2014; 69: 234-240.

29 Molstad S, Lofmark S, Carlin K, et al. Lessons learnt during 20 years of the Swedish strategic programme against antibiotic resistance. Bull World Health Organ. 2017; 95: 764-773.

30 Kalicki B, Milart J, Placzyńska M, et al. Borelioza - choroba nie tylko obszarów endemicznych - opis przypadku [Lyme borreliosis - not only endemic area disease - case report]. Pediatria i Medycyna Rodzinna. 2011; 7: 409-414.

31 Nitsch-Osuch A, Gyrczuk E, Wardyn A, et al. Antibiotics prescription practices among children with influenza. Adv Exp Med Biol. 2016; 905: 25-31.

32 Nyquist AC, Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for children with colds, upper respiratory tract infections and bronchitis. JAMA. 1998; 279: 875-878.

33 Ciesla G, Leader S, Stoddard J. Antibiotic prescribing rates in the US ambulatory care setting for patient diagnosed with influenza, 1997-2001. Respir Med. 2004; 98: 1093-1101.

34 Eccles R. An explanation for the seasonality of acute upper respiratory tract viral infections. Acta Otolaryngol. 2002; 122: 183-191.

35 Lipsitch M, Viboud C. Influenza seasonality: lifting the fog. Proc Natl Acad Sci U S A. 2009; 106: 3645-3646.

36 Lofgren E, Fefferman NH, Naumov YN, et al. Influenza seasonality: underlying causes and modeling theories. J Virol. 2007; 81: 5429-5436.

37 Kramarz P, Monnet D, Nicoll A, et al. Use of oseltamivir in 12 European countries between 2002 and 2007 - lack of association with the appearance of oseltamivir-resistant influenza A (H1N1) viruses. Euro Surveill. 2009; 14.

38 Low D. Reducing antibiotic use in influenza: challenges and rewards. Clin Microbiol Infect. 2008; 14: 298-306.

39 Ortiz JR, Kamimoto L, Aubert RE, et al. Oseltamivir prescribing in pharmacy-benefits database, United States, 2004-2005. Emerg Infect Dis. 2008; 14: 1280-1283.

40 Assink MDM, Kiewiet JP, Rozenbaum MH, et al. Excess drug prescriptions during influenza and RSV seasons in the Netherlands: potential implications for extended influenza vaccination. Vaccine. 2009; 27: 1119-1126.