J Antimicrob Chemother 2023; **78**: 2572–2580
https://doi.org/10.1093/jac/dkad273 Advance Access publication 6 September 2023

Journal of Antimicrobial Chemotherapy

Impact of the COVID-19 pandemic on community antibiotic consumption in the EU/European Economic Area: a changepoint analysis

Helene Vermeulen [1]*, Niel Hens [1,2,3], Lucy Catteau[4], Boudewijn Catry[4,5] and Samuel Coenen [2,3]

[1]Interuniversity Institute for Biostatistics and Statistical Bioinformatics (I-BIOSTAT), Data Science Institute (DSI), Hasselt University, Hasselt, Belgium; [2]Department of Family Medicine and Population Health (FAMPOP), University of Antwerp, Antwerp, Belgium; [3]Vaccine and Infectious Disease Institute (VAXINFECTIO), University of Antwerp, Antwerp, Belgium; [4]Department of Epidemiology and Public Health, Sciensano, Brussels, Belgium; [5]Faculty of Medicine, Université libre de Bruxelles (ULB), Brussels, Belgium

*Corresponding author. E-mail: helene.vermeulen@uhasselt.be

Received 6 March 2023; accepted 21 August 2023

Objectives: A decrease in community antibiotic consumption in Europe has been observed during the COVID-19 pandemic. The magnitude of this decrease, how fast after the outbreak it occurred, whether it was sustained during the pandemic and whether the seasonal variation in antibiotic consumption was affected, have not yet been evaluated in detail.

Methods: Data on community antibiotic consumption were available from the European Surveillance of Antimicrobial Consumption Network for 28 EU/European Economic Area (EEA) countries between 2010 and 2021. Antibiotic consumption was expressed as DDDs per 1000 inhabitants per day (DID). The impact of the pandemic on antibiotic consumption was investigated using descriptive statistics and non-linear mixed changepoint models for quarterly and yearly data.

Results: The decrease in overall antibiotic consumption between 2019 and 2020 (−3.4 DID; −18.6%) was mainly due to a decrease in the consumption of penicillins [Anatomical Therapeutic Chemical (ATC) code J01C] (−1.9 DID; −23.0%), other β-lactam antibacterials (J01D) (−0.6 DID; −25.8%) and macrolides, lincosamides and streptogramins (J01F) (−0.5 DID; −17.4%) and was sustained during 2021. The changepoint analysis of yearly data (28 countries) estimated a decrease of 3.3 DID in overall antibiotic consumption (J01) between 2019 and 2020. The analysis of quarterly data (16 countries) estimated a decrease in overall antibiotic consumption (J01) of 4.0 DID and a decrease in seasonal variation of 1.2 DID between the first and second quarters of 2020.

Conclusions: The changepoint analysis indicated a significant, sudden and steep decrease in community antibiotic consumption in the EU/EEA immediately after the start of the COVID-19 outbreak in Europe, as well as a decrease in its seasonal variation.

Introduction

On 11 March 2020, the WHO declared the COVID-19 pandemic, which resulted in numerous deaths globally.[1] Alongside the COVID-19 pandemic, Europe is also suffering a considerable number of deaths from the silent but equally serious pandemic caused by antibiotic-resistant pathogens. Antimicrobial resistance (AMR), resulting from overuse and inappropriate use of antibiotics, is a major global health issue.[2] The majority of antibiotics in Europe are used in the community (i.e. primary care). In order to fight the problem of AMR, reliable data on antibiotic consumption in the community are needed. The European Surveillance of Antimicrobial Consumption Network (ESAC-Net), coordinated by the ECDC, collects data on community consumption of antibiotics for 28 EU/European Economic Area (EEA) countries.[3] According to these data, a decrease in the consumption of antibiotics has been observed during the COVID-19 pandemic,[4] whereas antibiotic consumption in the EU/EEA had remained stable for at least 20 years.[5] However, the observed decrease has not yet been assessed in detail, using changepoint models that allow establishment of the magnitude of the decrease, how fast after the COVID-19 outbreak the decrease occurred, whether it was sustained during the pandemic and whether the seasonal variation of antibiotic consumption was affected during the COVID-19 pandemic. Therefore, this study examined the decrease in antibiotic consumption throughout the COVID-19 pandemic in Europe using changepoint models.

Methods

Data

Data on the consumption of antibiotics [Anatomical Therapeutic Chemical (ATC) code J01; version 2021][6] in the community were available from the ESAC-Net for 28 EU/EEA countries between 2010 and 2021 and were retrieved from the ECDC through the European Surveillance System (TESSy) in December 2022 in accordance with the ESAC-Net reporting protocol.[7] Nine countries reported quarterly data, 7 countries reported quarterly data and yearly data, depending on the year of reporting, and 12 countries reported yearly data only. Not all countries reported community data for all years. Table S1 (available as Supplementary data at *JAC* Online) gives an overview of the type of data available for each of the countries by year. Antibiotic consumption was expressed as DDD per 1000 inhabitants per day (DID) for each antibiotic subclass aggregated at the level of the active substance in accordance with the WHO ATC classification (ATC level 3).[6] Due to the limited DDDs reported for amphenicols (J01B), aminoglycoside antibacterials (J01G) and combinations of antibacterials (J01R), data on these antibiotics were combined and referred to as 'low consumption antibacterials'. Denominator data from Eurostat were used to calculate DID values. Reported DID values might thus slightly differ from those reported by ESAC-Net. Finally, the DID values were corrected for incomplete coverage.[8]

Analysis

The consumption of antibiotics, expressed in DID, was calculated for each of the 28 EU/EEA countries from 2010 until 2021, and the change in antibiotic consumption between 2019 and 2020, and 2020 and 2021, was calculated to evaluate the impact of the COVID-19 pandemic on community consumption in Europe and each of the 28 EU/EEA countries. The antibiotic subclasses substantially contributing to the decrease in overall antibiotic consumption (J01) were identified, and the impact of the COVID-19 pandemic on the consumption of these subclasses, as well as on overall antibiotic consumption (J01), was further investigated using non-linear mixed changepoint models with a sine function to catch seasonality, as described by Bruyndonckx *et al.*[9] Besides, to assess the appropriateness of the antibiotics used during the COVID-19 pandemic in the EU/EEA community, the percentage of Access antibiotics was calculated in 2019, 2020 and 2021, as defined by the Access, Watch, Reserve (AWaRe) classification system of the WHO.[10] Finally, the use of azithromycin was investigated separately at ATC level 5 due to its encouraged use during the beginning of the COVID-19 pandemic.

To assess the seasonal variation in antibiotic consumption and to accurately estimate the changepoint, i.e. the moment antibiotic consumption decreased, the changepoint models were applied to data from countries reporting mainly quarterly. Consequently, data from 16 countries, i.e. Austria, Belgium, Croatia, Czechia, Denmark, Estonia, Finland, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Luxembourg, Portugal and Slovenia, were included in the analysis. Fourteen of these countries provided quarterly data in 2019–2021, allowing a more accurate estimation of the changepoint. Yet, to estimate the actual magnitude of the decrease in the consumption of antibiotics, an additional analysis was performed including the yearly data from all 28 EU/EEA countries.

In the changepoint analyses, models containing one or two changepoints were fitted and model selection was performed using the deviance information criterion, where a lower value indicates a better model fit.[11] The most elaborate model with one changepoint included: (i) a change in intercept, i.e. a sudden decrease or increase in antibiotic consumption; (ii) a change in slope, i.e. a decreasing or increasing trend in antibiotic consumption; and (iii) a change in amplitude, i.e. a decrease or increase in the seasonal variation of antibiotic consumption. Further, this model included a random intercept, slope and amplitude, as well as a random change in intercept, slope and amplitude to allow for country-specific evolutions and changes, respectively. The most elaborate model with two changepoints included: (i) two changes in intercept; (ii) two changes in slope; and (iii) two changes in amplitude, as well as a random intercept, slope and amplitude, and random changes in intercept, slope and amplitude. All other models fitted in the analyses were simplifications of those models in which particular terms were excluded. Bayesian model fitting was applied in order to determine the changepoints in a data-driven manner, allowing assessment of how soon after the emergence of the COVID-19 pandemic a change in antibiotic consumption occured.[12] Further details on the model structures and model fitting can be found in the Supplementary material.

Results

In Europe (27 EU/EEA countries; no data for Czechia in 2019 and 2020), a decrease in the overall antibiotic consumption (J01) in the community was observed from 18.36 DID in 2019 to 14.95 DID in 2020 (−18.57%) (Table 1). This decrease in overall antibiotic consumption was mainly due to the decrease in other β-lactam antibacterials (J01D), penicillins (J01C) and macrolides, lincosamides and streptogramins (J01F), where a decrease of 25.78%, 22.97% and 17.42% was observed, respectively. The consumption of quinolone antibacterials (J01M) decreased by 14.89%. A decrease of 7.27% was observed in the consumption of sulfonamides and trimethoprim (J01E). The consumption of low consumption antibacterials (J01B, J01G and J01R) decreased by 7.14%. The decrease observed in the consumption of tetracyclines (J01A) was 6.86%, and the consumption of other antibacterials (J01X) decreased by 2.91%. The decrease in overall antibiotic consumption (J01) in the community was sustained in 2021 (28 EU/EEA countries), where overall antibiotic use rose only slightly to 14.98 DID (+0.20%). The consumption of other antibacterials (J01X), tetracyclines (J01A), penicillins (J01C) as well as macrolides, lincosamides and streptogramins (J01F) increased by 3.00%, 2.45%, 1.24% and 0.42%, respectively. The consumption of low consumption antibacterials (J01B, J01G and J01R), other β-lactam antibacterials (J01D) and quinolone antibacterials (J01M) further decreased in 2021 by 7.69%, 4.79% and 3.33%, respectively. No change was observed in the consumption of sulfonamides and trimethoprim (J01E). Although overall antibiotic consumption decreased in Europe between 2019 and 2020, increases in the use of separate antibiotic subclasses were observed for several countries. An overview of the changes in antibiotic consumption between 2019 and 2020 is given in Table S2 for each antibiotic subclass and country. The proportion of Access antibiotics used in the EU/EEA community slightly increased from 63.25% in 2019 to 63.53% in 2020 and 64.27% in 2021. The proportions of Access antibiotics used in 2019–2021 for each country are given in Table S3.

From 2019 to 2020, a decrease in overall antibiotic consumption (J01) was observed for each of the separate countries, except for Bulgaria, where the overall antibiotic consumption (J01) increased by 8.81%. The largest decrease in overall consumption (J01) was observed in Austria (−27.23%), whereas the smallest decrease was observed in Romania (−1.21%). Overall antibiotic consumption remained stable in most countries in 2021, with only small changes from 2020 to 2021. Between 2020 and 2021, overall antibiotic consumption rose in 15 countries and decreased in 12 countries. The largest increase was

Table 1. Changes in overall antibiotic consumption (J01) and the consumption of each antibiotic subclass, expressed in DDD per 1000 inhabitants per day in the EU/EEA (2019–2021)

				2019 versus 2020		2020 versus 2021	
	2019	2020	2021	Absolute change	Relative change	Absolute change	Relative change
Overall consumption of antibiotics (J01)	18.36	14.95	14.98	−3.41	−18.57%	+0.03	+0.20%
Penicillins (J01C)	8.36	6.44	6.52	−1.92	−22.97%	+0.08	+1.24%
Macrolides, lincosamides and streptogramins (J01F)	2.87	2.37	2.38	−0.50	−17.42%	+0.01	+0.42%
Other β-lactam antibacterials (J01D)	2.25	1.67	1.59	−0.58	−25.78%	−0.08	−4.79%
Tetracyclines (J01A)	1.75	1.63	1.67	−0.12	−6.86%	+0.04	+2.45%
Quinolone antibacterials (J01M)	1.41	1.20	1.16	−0.21	−14.89%	−0.04	−3.33%
Other antibacterials (J01X)	1.03	1.00	1.03	−0.03	−2.91%	+0.03	+3.00%
Sulfonamides and trimethoprim (J01E)	0.55	0.51	0.51	−0.04	−7.27%	0.00	0.00%
Low consumption antibacterials (J01B, J01G and J01R)	0.14	0.13	0.12	−0.01	−7.14%	−0.01	−7.69%

No data were available for Czechia in 2019 and 2020. In 2021, data from all 28 EU/EEA countries were available.

observed in Slovakia (+10.49%) and the largest decrease was observed in Greece (−17.41%). The changes in overall antibiotic consumption (J01) from 2019 until 2021 are given in Table 2 for each of the separate countries.

The increase in overall antibiotic consumption (J01) between 2019 and 2020 in Bulgaria was mainly due to an increase in the use of macrolides, lincosamides and streptogramins (J01F), predominantly caused by the increase of azithromycin (J01FA10), which more than doubled (+1.60 DID, +104.58%). An increase in the use of azithromycin (J01FA10) has also been observed in Greece, France, Ireland, Italy, Lithuania and Romania. However, over all 28 EU/EEA countries, the consumption of azithromycin slightly decreased by 0.89% (−0.01 DID). An overview of the changes in azithromycin (J01FA10) consumption between 2019, 2020 and 2021 is given in Table 3 for each country.

Changepoint analysis

Overall consumption of antibiotics (J01)

According to the analysis of the data from the 16 EU/EEA countries providing quarterly data, a model containing a change in intercept and amplitude was the best fit to describe the decrease in overall antibiotic consumption (J01) (Table 4). The overall antibiotic consumption (J01) in 2010 in EU/EEA countries reporting quarterly data was estimated at 16.02 DID [95% credible interval (CrI): 14.04, 18.17] and did not change over time until the changepoint between the first and second quarter of 2020. Between the first and second quarter of 2020, the overall consumption (J01) decreased by 4.03 DID (95% CrI: 3.18, 4.88). This decrease was significantly smaller than average in Estonia and Latvia and larger in Belgium and Finland. The analysis further showed significant seasonal variation, with an amplitude of 2.66 DID (95% CrI: 2.04, 3.27), which decreased after the changepoint by 1.24 DID (95% CrI: 0.36, 2.11). The decrease in seasonal variation after the changepoint did not differ between countries.

According to the analysis of the yearly data from all 28 EU/EEA countries, a model containing a change in intercept was the best fit to describe the decrease in the overall antibiotic consumption (J01) (Table 4). The overall antibiotic consumption (J01) in the EU/EEA in 2010 was estimated at 17.24 DID (95% CrI: 15.51, 18.96) and did not change over time until the changepoint between 2019 and 2020. Between 2019 and 2020, the overall consumption of antibiotics (J01) decreased by 3.27 DID (95% CrI: 2.36, 4.17). This decrease was significantly larger than average in Greece, Luxembourg, Poland, Slovakia and Spain and smaller in Denmark, the Netherlands, Norway, Romania and Sweden, whereas in Bulgaria an increase in overall antibiotic use was observed.

Consumption of penicillins (J01C)

According to the analysis of the data from the 16 EU/EEA countries providing quarterly data, a model containing a change in intercept and amplitude was the best fit to describe the decrease in penicillin (J01C) consumption (Table 4). Consumption of penicillins (J01C) in 2010 in the EU/EEA countries reporting quarterly data was estimated at 6.89 DID (95% CrI: 5.72, 8.32) and did not change over time until the changepoint between the first and second quarter of 2020. Between the first and second quarter of 2020, the consumption of penicillins (J01C) decreased by 1.83 DID (95% CrI: 1.37, 2.29). This decrease was significantly smaller than average in Denmark and Estonia, and larger in Belgium and Ireland. The analysis further showed significant seasonal variation, with an amplitude of 1.16 DID (95% CrI: 0.87, 1.45), which decreased after the changepoint by 0.67 DID (95% CrI: 0.17, 1.16). After the changepoint, the seasonal variation significantly increased in Italy.

According to the analysis of the yearly data from all 28 EU/EEA countries, a model containing two changepoints was the best fit to describe the decrease in penicillin (J01C) consumption (Table 4). Between 2015 and 2016, a small increase in the consumption of penicillins (J01C) was identified in the EU/EEA.

Table 2. Change in overall antibiotic consumption (J01) expressed in DDD per 1000 inhabitants per day for each EU/EEA country (2019–2021)

				2019 versus 2020		2020 versus 2021	
	2019	2020	2021	Absolute change	Relative change	Absolute change	Relative change
Austria	9.77	7.11	7.19	−2.66	−27.23%	+0.08	+1.13%
Belgium	19.77	15.25	16.00	−4.52	−22.86%	+0.75	+4.92%
Bulgaria	19.06	20.74	22.36	+1.68	+8.81%	+1.62	+7.81%
Croatia	17.80	14.83	15.63	−2.97	−16.69%	+0.80	+5.39%
Czechia	—	—	11.52	—	—	—	—
Denmark	13.44	12.51	12.59	−0.93	−6.92%	+0.08	+0.64%
Estonia	10.24	8.81	8.66	−1.43	−13.96%	−0.15	−1.70%
Finland	12.56	9.95	9.45	−2.61	−20.78%	−0.50	−5.03%
France	23.25	18.63	19.87	−4.62	−19.87%	+1.24	+6.66%
Germany	11.36	8.97	8.15	−2.39	−21.04%	−0.82	−9.14%
Greece	32.41	26.37	21.78	−6.04	−18.64%	−4.59	−17.41%
Hungary	13.27	10.03	10.82	−3.24	−24.42%	+0.79	+7.88%
Iceland	17.96	15.38	15.73	−2.58	−14.37%	+0.35	+2.28%
Ireland	21.02	17.09	16.31	−3.93	−18.70%	−0.78	−4.56%
Italy	19.98	16.50	15.99	−3.48	−17.42%	−0.51	−3.09%
Latvia	12.02	9.97	10.16	−2.05	−17.05%	+0.19	+1.91%
Lithuania	13.83	11.92	11.70	−1.91	−13.81%	−0.22	−1.85%
Luxembourg	19.90	14.94	14.71	−4.96	−24.92%	−0.23	−1.54%
Malta	18.71	14.38	14.11	−4.33	−23.14%	−0.27	−1.88%
Netherlands	8.73	7.74	7.61	−0.99	−11.34%	−0.13	−1.68%
Norway	13.61	12.76	12.84	−0.85	−6.25%	+0.08	+0.63%
Poland	22.23	17.15	18.83	−5.08	−22.85%	+1.68	+9.80%
Portugal	17.07	13.06	13.16	−4.01	−23.49%	+0.10	+0.77%
Romania	24.04	23.75	24.28	−0.29	−1.21%	+0.53	+2.23%
Slovakia	17.97	13.15	14.53	−4.82	−26.82%	+1.38	+10.49%
Slovenia	11.54	8.86	8.74	−2.68	−23.22%	−0.12	−1.35%
Spain	23.46	18.21	18.49	−5.25	−22.38%	+0.28	+1.54%
Sweden	10.33	8.92	8.66	−1.41	−13.65%	−0.26	−2.91%

No data were available for Czechia in 2019 and 2020.

However, this increase was not statistically significant at the European level. Community consumption in 2010 was estimated at 6.96 DID (95% CrI: 6.05, 7.79) and thus did not significantly change over time in the EU/EEA until the second changepoint between 2019 and 2020, where the consumption of penicillins (J01C) suddenly and significantly decreased by 1.74 DID (95% CrI: 1.36, 2.12). The decrease between 2019 and 2020 was significantly larger than average in France, Greece, Ireland and Spain, and smaller in Bulgaria, Estonia, the Netherlands and Norway. Although, on average, no significant change was observed in the use of penicillins (J01C) in the EU/EEA between 2015 and 2016, their consumption significantly increased in Greece and Spain and decreased in Ireland, Italy and Luxembourg.

Consumption of other β-lactam antibacterials (J01D)

According to the analysis of the data from the 16 EU/EEA countries providing quarterly data, a model with a change in intercept and amplitude was the best fit to describe the decrease in other β-lactam antibacterials (J01D) (Table 4). Consumption of other β-lactam antibacterials (J01D) in 2010 in the EU/EEA countries reporting quarterly data was estimated at 1.58 DID (95% CrI: 1.07, 2.04) and did not change over time until the changepoint between the first and second quarters of 2020. Between the first and second quarters of 2020, the consumption of other β-lactam antibacterials (J01D) suddenly decreased by 0.46 DID (95% CrI: 0.22, 0.69). This decrease was significantly smaller than average in Denmark, Iceland and Slovenia and larger in Germany. The analysis further showed significant seasonal variation, with an amplitude of 0.35 DID (95% CrI: 0.17, 0.51), which decreased after the changepoint by 0.23 DID (95% CrI: 0.12, 0.34). The decrease in seasonal variation after the changepoint did not differ between countries.

According to the analysis of the yearly data from all 28 EU/EEA countries, a model containing a change in intercept was the best fit to describe the decrease in other β-lactam antibacterials (J01D) (Table 4). According to this model, consumption of other β-lactam antibacterials (J01D) in the EU/EEA in 2010 was estimated at 2.10 DID (95% CrI: 1.43, 2.74) and did not change over time until the changepoint between 2019 and 2020. Between 2019 and 2020, the consumption of other β-lactam

Table 3. Change in azithromycin consumption (J01FA10) expressed in DDD per 1000 inhabitants per day for each EU/EEA country (2019–2021)

				2019 versus 2020		2020 versus 2021	
	2019	2020	2021	Absolute change	Relative change	Absolute change	Relative change
Austria	0.73	0.46	0.48	−0.27	−36.99%	+0.02	+4.35%
Belgium	1.98	1.58	1.64	−0.40	−20.20%	+0.06	+3.80%
Bulgaria	1.53	3.13	3.21	+1.60	+104.58%	+0.08	+2.56%
Croatia	1.67	1.59	1.94	−0.08	−4.79%	+0.35	+22.01%
Czechia	—	—	0.71	—	—	—	—
Denmark	0.53	0.41	0.49	−0.12	−22.64%	+0.08	+19.51%
Estonia	0.56	0.48	0.51	−0.08	−14.29%	+0.03	+6.25%
Finland	0.27	0.17	0.15	−0.10	−37.04%	−0.02	−11.76%
France	0.73	0.86	0.90	+0.13	+17.81%	+0.04	+4.65%
Germany	0.53	0.35	0.31	−0.18	−33.96%	−0.04	−11.43%
Greece	1.42	1.62	1.40	+0.20	+14.08%	−0.22	−13.58%
Hungary	1.39	1.14	1.77	−0.25	−17.99%	+0.63	+55.26%
Iceland	0.88	0.68	0.68	−0.20	−22.73%	0.00	0.00%
Ireland	1.05	1.06	0.95	+0.01	+0.95%	−0.11	−10.38%
Italy	1.53	1.77	1.71	+0.24	+15.69%	−0.06	−3.39%
Latvia	0.51	0.45	0.55	−0.06	−11.76%	+0.10	+22.22%
Lithuania	0.44	0.46	0.39	+0.02	+4.55%	−0.07	−15.22%
Luxembourg	1.23	0.97	0.99	−0.26	−21.14%	+0.02	+2.06%
Malta	1.47	1.11	1.15	−0.36	−24.49%	+0.04	+3.60%
Netherlands	0.91	0.87	0.83	−0.04	−4.40%	−0.04	−4.60%
Norway	0.21	0.16	0.17	−0.05	−23.81%	+0.01	+6.25%
Poland	1.64	1.14	1.80	−0.50	−30.49%	+0.66	+57.89%
Portugal	1.67	1.07	1.00	−0.60	−35.93%	−0.07	−6.54%
Romania	1.08	2.99	2.53	+1.91	+176.85%	−0.46	−15.38%
Slovakia	1.66	1.27	2.28	−0.39	−23.49%	+1.01	+79.53%
Slovenia	0.79	0.65	0.60	−0.14	−17.72%	−0.05	−7.69%
Spain	1.96	1.44	1.40	−0.52	−26.53%	−0.04	−2.78%

No data were available for Czechia in 2019 and 2020. Community data were not available at ATC level 5 for Sweden.

antibacterials (J01D) suddenly decreased by 0.54 DID (95% CrI: 0.29, 0.81). This decrease was significantly smaller than average in Denmark, the Netherlands, Norway, Slovenia and Sweden, and larger in Germany, Greece, Poland and Slovakia.

Consumption of macrolides, lincosamides and streptogramins (J01F)

According to the analysis of the data from the 16 EU/EEA countries providing quarterly data, a model with a change in intercept and amplitude was the best fit to describe the decrease in macrolides, lincosamides and streptogramins (J01F) (Table 4). Consumption of macrolides, lincosamides and streptogramins (J01F) in 2010 in the EU/EEA countries reporting quarterly data was estimated at 2.77 DID (95% CrI: 2.25, 3.29) and did not change over time until the changepoint between the first and second quarters of 2020. Between the first and second quarters of 2020, the consumption of macrolides, lincosamides and streptogramins (J01F) suddenly decreased by 0.86 DID (95% CrI: 0.62, 1.11). This decrease was significantly smaller than average in Croatia and larger in Austria and Ireland. The analysis further showed significant seasonal variation, with an amplitude of 0.77 DID (95% CrI: 0.58, 0.96), which decreased after the changepoint by 0.32 DID (95% CrI: 0.14, 0.50). The decrease in seasonal variation after the changepoint did not differ between countries.

According to the analysis of the yearly data from all 28 EU/EEA countries, a model containing a change in intercept was the best fit to describe the decrease in macrolides, lincosamides and streptogramins (J01F) (Table 4). According to this model, consumption of macrolides, lincosamides and streptogramins (J01F) in the EU/EEA in 2010 was estimated at 3.09 DID (95% CrI: 2.44, 3.74) and did not change over time until the changepoint between 2019 and 2020. Between 2019 and 2020, the consumption of macrolides, lincosamides and streptogramins (J01F) suddenly decreased by 0.54 DID (95% CrI: 0.22, 0.86). This decrease was significantly smaller than average in Romania, and larger in Greece, Ireland, Luxembourg, Malta and Poland, whereas in Bulgaria a significant increase was observed.

Discussion

After a relatively stable decade, a sudden and large decrease in overall antibiotic consumption was observed in the EU/EEA

Table 4. Consumption of antibiotics (stratified by class) in the community, 2010–2021: parameter estimates and 95% credible intervals (CrI) based on changepoint analyses of quarterly data (16 EU/EEA countries) and yearly data (28 EU/EEA countries)

	Overall antibiotic consumption (J01)		Penicillins (J01C)		Other β-lactam antibacterials (J01D)		Macrolides, lincosamides and streptogramins (J01F)	
	Quarterly data	Yearly data	Quarterly data	Yearly data	Quarterly data	Yearly data	Quarterly data	Yearly data
Intercept	16.02 (14.04, 18.17)	17.24 (15.51, 18.96)	6.89 (5.72, 8.32)	6.96 (6.05, 7.79)	1.58 (1.07, 2.04)	2.10 (1.43, 2.74)	2.77 (2.25, 3.29)	3.09 (2.44, 3.74)
Change in intercept	−4.03 (−4.88, −3.18)	−3.27 (−4.17, −2.36)	−1.83 (−2.29, −1.37)	**CP1:** 0.12 (−0.35, 0.59) **CP2:** −1.74 (−2.12, −1.36)	−0.46 (−0.69, −0.22)	−0.54 (−0.81, −0.29)	−0.86 (−1.11, −0.62)	−0.54 (−0.86, −0.22)
Slope	NI	−0.01 (−0.15, 0.14)	NI	0.03 (−0.03, 0.08)	NI	0.00 (−0.04, 0.05)	NI	−0.03 (−0.07, 0.01)
Change in slope	NI	NI	NI	NI	NI	NI	NI	NI
Seasonal variation	2.66 (2.04, 3.27)	NI	1.16 (0.87, 1.45)	NI	0.35 (0.17, 0.51)	NI	0.77 (0.58, 0.96)	NI
Change in seasonal variation	−1.24 (−2.11, −0.36)	NI	−0.67 (−1.16, −0.17)	NI	−0.23 (−0.34, −0.12)	NI	−0.32 (−0.50, −0.14)	NI
Changepoint	Between first and second quarters of 2020	Between 2019 and 2020	Between first and second quarters of 2020	**CP1:** Between 2015 and 2016 **CP2:** Between 2019 and 2020	Between first and second quarters of 2020	Between 2019 and 2020	Between first and second quarters of 2020	Between 2019 and 2020

Intercept: consumption in the first quarter of 2010. Change in intercept: sudden increase/decrease in consumption at the changepoint. Slope: gradual increase/decrease in consumption per quarter/year before changepoint. Change in slope: difference in slope after versus before the changepoint. Seasonal variation: magnitude of the upward winter and downward summer peak in consumption. Change in seasonal variation: increase/decrease of the magnitude of the upward winter and downward summer peak in consumption. Changepoint: timing of the changepoint. CP, changepoint, NI, not included.

community between 2019 and 2020, which was sustained during 2021. The antibiotic subclasses most frequently used in Europe, i.e. penicillins (J01C), other β-lactam antibacterials (J01D) and macrolides, lincosamides and streptogramins (J01F) together accounted for 86.24% of the overall decrease. The decrease in antibiotic use occurred immediately after the start of the COVID-19 outbreak in Europe, i.e. between the first and second quarters of 2020, after which the seasonal variation of overall antibiotic consumption (J01) and of the most frequently used antibiotic subclasses also decreased. The proportion of Access antibiotics used during the COVID-19 pandemic in Europe remained stable over time and reached the threshold of 60% set by the WHO.[10] These results indicate that although antibiotic use decreased in the European community during the pandemic, the prescribed antibiotics were still in line with the WHO's overarching goals of promoting responsible antibiotic consumption.

Similar decreases in community antibiotic consumption have been described in previous national studies conducted within as well as outside Europe, whereas increases in community antibiotic consumption were only rarely observed.[12] In Navarre, Spain, a decrease of 39% in community antibiotic consumption was observed when comparing the second quarter of 2019 and 2020. This study also concluded that seasonality in the use of community antibiotics disappeared.[13] A decrease of 28% in the community consumption of antibiotics was observed between 2019 and 2020 in an Italian study.[14] In the UK, a decreasing trend in antibiotic use in the community was observed before the onset of the COVID-19 pandemic, which further decreased as of March 2020 and was sustained during winter, in contrast to the seasonality in antibiotic prescribing that was previously observed within the UK.[15,16] The community consumption of antibiotics in the USA decreased by 26.8% between March and December 2020 compared with the same period in 2017–2019.[17] In Canada, antibiotic consumption in the community decreased by 26.5% between March and October 2020.[18] A decrease of 36% in community antibiotic consumption was observed as of April 2020 in Australia, which persisted into winter (June–August), again pointing out decreased seasonality.[19] In Hong Kong, antibiotic supplies to community pharmacies decreased by 47.9% between 2019 and 2021.[20] A study conducted in South Korea found a decrease in antibiotic community consumption of 14%–30% compared with the three preceding years, after adjusting for the observed decrease in respiratory tract infections (RTIs) during the COVID-19 pandemic.[21]

Indeed, a decrease in (non-COVID-19) RTIs during the COVID-19 pandemic has been observed in several countries, often coinciding with the decrease in antibiotic use in the community. These studies also show that the decrease in community antibiotic consumption is mainly due to a decrease in the consumption of antibiotics used to treat RTIs.[13,15,18,19,21] Although to a lesser extent, a decrease in other communicable diseases has been observed, further explaining the decrease in antibiotic use. Reduced disease transmission during the COVID-19 pandemic resulted from a variety of non-pharmaceutical interventions, such as lockdowns, travel restrictions, school closures, the use of face masks, increased hand hygiene, social distancing, etc. Finally, the decrease in antibiotic use in the community might also be the result of hesitancy to seek medical care in case of mild symptoms. These results show that there is room for improvement in the prescription of antibiotics for respiratory infections, which are often of viral origin.

An increase in the use of azithromycin (J01FA10) has been observed for several countries. Azithromycin is an antibiotic that has shown *in vitro* activity against the SARS-CoV-2 virus.[22] Besides, results from a non-randomized clinical trial published in early 2020 indicated that azithromycin, in combination with hydroxychloroquine, significantly reduced the viral load in COVID-19 patients.[23] However, this study suffers from major methodological issues concerning the design of the trial, the outcome measure and the statistical analyses, as discussed by Rosendaal[24] and Machiels *et al*.[25] Moreover, several studies later demonstrated that the treatment of COVID-19 with azithromycin, in addition to standard care or hydroxychloroquine treatment, did not reduce the symptoms, nor the risk for hospitalization or death in outpatients.[26–29]

A positive correlation between antibiotic use and AMR levels has been demonstrated by multiple studies.[30–35] Unless the persistence of AMR has a selective advantage, the observed decrease in community antibiotic consumption might result in a decrease in the AMR levels of community pathogens in the EU/EEA. Although literature on the impact of the COVID-19 pandemic on AMR levels in the community is scarce, Tedeschi *et al*.[14] showed an improvement in AMR patterns in the out-of-hospital setting following the decreased community use of antibiotics during the COVID-19 pandemic. Lemenand *et al*.[36] showed a decrease in the proportion of ESBL-producing *Escherichia coli* infections during the COVID-19 pandemic. These studies seem to support the hypothesis of a decrease in AMR due to decreased antibiotic use in the community. However, the latest annual epidemiological report on AMR in the EU/EEA by the European Antimicrobial Resistance Surveillance Network (EARS-Net) indicates that the changes in AMR levels during the COVID-19 pandemic vary greatly between different bacterial species, antimicrobial agents and countries.[37] It has to be noted, however, that most pathogens under surveillance by EARS-Net are found in hospitalized patients, that they are unlikely to be affected by community antibiotic consumption and that not all drug-bug combinations are considered. Besides, a lag is expected between the decrease in antibiotic use and its effect on AMR.[38] Therefore, the impact of decreased antibiotic consumption, as a result of the COVID-19 pandemic, on AMR levels in the community remains an interesting topic for future research.

Strengths and limitations

We estimated the magnitude, timing and persistence of the decrease in antibiotic consumption in the European community during the COVID-19 pandemic using non-linear mixed changepoint models. Quarterly data enabled estimation of the timing of the decrease as well as the seasonal variation in antibiotic use. However, only 16 of 28 countries reported on antibiotic use quarterly, potentially biasing the estimated seasonal variation in Europe. We therefore believe reporting quarterly data should be encouraged. The observed decrease in antibiotic use was sustained during 2021. However, whether the use of antibiotics returns to pre-pandemic levels in 2022 or 2023 remains to be evaluated.

Conclusion

In conclusion, our analysis indicated a significant, sudden and steep decrease in overall antibiotic consumption in the European community between the first and second quarters of 2020, as well as a decrease in its seasonal variation. Although consumption in the European community remained low during 2021, it remains to be seen how it will evolve in post-pandemic times.

Acknowledgements

We would like to thank Vivian Leung for providing the ESAC-Net data, and Liselotte Diaz Högberg and Dominique Monnet for their valuable feedback on the manuscript. Further, we would like to acknowledge the staff of the national healthcare services that provided data to the European Surveillance of Antimicrobial Consumption Network, for their engagement in collecting, validating and reporting antimicrobial consumption data.

Funding

This work was supported by the Methusalem funding programme of the Flemish Government. N.H. acknowledges support from the University of Antwerp scientific chair in Evidence-Based Vaccinology.

Transparency declarations

The views and opinions of the authors expressed herein do not necessarily state or reflect those of the ECDC. The accuracy of the authors' statistical analysis and the findings they report are not the responsibility of the ECDC. The ECDC is not responsible for conclusions or opinions drawn from the data provided, neither is it responsible for the correctness of the data and for data management, data merging and data collation after provision of the data. The ECDC shall not be held liable for improper or incorrect use of the data.

Supplementary data

Tables S1 to S3 and Supplementary material are available as Supplementary data at *JAC* Online.

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