Vermeulen *et al. Archives of Public Health* (2024) 82:197
https://doi.org/10.1186/s13690-024-01427-w

Archives of Public Health

CORRESPONDENCE

Open Access

Community antibiotic consumption in the European Union/European economic area: late-pandemic rebound and seasonality analysis

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Abstract

Background A rebound in antibiotic consumption has been observed in the European community at the end of the COVID-19 pandemic. Here we evaluate the extent of this increase, when it exactly occurred, and how the seasonality in antibiotic use changed during the late-pandemic period.

Methods Data on community antibiotic consumption were available from the European Surveillance of Antimicrobial Consumption Network for 28 European countries between 2015 and 2022. Antibiotic consumption was expressed as defined daily doses per 1000 inhabitants per day (DID). The evolution in antibiotic use was investigated using non-linear changepoint mixed models for quarterly and yearly data.

Results An increase in overall antibiotic consumption was found in Europe between 2021 and 2022, mainly due to an increase in the consumption of penicillins, macrolides, lincosamides and streptogramins, and other β-lactam antibacterials. The analysis of quarterly data estimated a gradual increase in overall antibiotic consumption of 0.55 DID per quarter, as of the second quarter of 2020 and a decrease in seasonal variation of 1.64 DID between the first and second quarter of 2020. The changepoint analysis of yearly data estimated an increase of 3.33 DID in overall antibiotic consumption between 2021 and 2022.

Conclusions A gradual but significant rebound in the use of antibiotics was found in Europe, along with a decrease in its seasonal variation. The rapid rise in antibiotic consumption above pre-pandemic levels in several countries underlines the importance of continued antimicrobial stewardship.

Keywords Antibiotic use, Seasonality, Community, Europe, COVID-19

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Text box 1. Contributions to the literature

- An increase in antibiotic use has been observed during the late-pandemic period, but it has not yet been evaluated when this increase exactly took place, or how the seasonality in antibiotic use changed during the late-pandemic period.
- Analyses of quarterly data show a gradual increase in antibiotic use and a decrease in its seasonality, as of the second quarter of 2020, indicating inappropriate antibiotic use in the treatment of viral infections during the pre-pandemic period.
- Reporting quarterly data should be encouraged to improve the accuracy of future studies on antibiotic use.

Introduction

The European Surveillance of Antimicrobial Consumption Network (ESAC-Net), coordinated by the European Centre for Disease Prevention and Control (ECDC), monitors the antibiotic community consumption across 28 European Union/European Economic Area (EU/EEA) countries [1]. Based on these data, several studies showed an abrupt decrease in the use of antibiotics in the European community, shortly after the start of the COVID-19 pandemic in March 2020, as well as a decrease in the seasonality observed in their consumption [2, 3]. In 2022, at the end of the COVID-19 pandemic, the consumption of antibiotics in the European community returned to pre-pandemic levels and the year after, in May 2023, the WHO declared an end to COVID-19 as a public health emergency [4, 5]. However, it has not yet been evaluated when this increase in antibiotic community consumption exactly took place, and how the seasonality of antibiotic use changed during the late-pandemic period. Therefore, this study investigates antibiotic use in the European community during the COVID-19 pandemic, using changepoint models.

Methods

Data

Data on antibiotic community consumption were available from ESAC-Net for 28 EU/EEA countries between 2015 and 2022 and were retrieved from the ECDC through the European Surveillance System (TESSy) in January 2024 [6]. Twelve countries reported quarterly data, 4 countries reported quarterly and yearly data, depending on the year of reporting, and 12 countries reported yearly data. Not all countries reported on their community consumption for all years. Supplementary table S1gives an overview of the type of data available for each country by year. Antibiotic consumption was expressed as defined daily doses (DDDs) per 1000 inhabitants per day (DID) for each antibiotic subclass aggregated at the level of the active substance (Anatomical Therapeutic Chemical (ATC) code level 3) [7]. DDDs were extrapolated to cover 100% consumption in case of incomplete coverage and denominator data from Eurostat were used to calculate DID values [8]. Reported DID values might thus slightly differ from those reported by ESAC-Net.

Analysis

Antibiotic consumption was calculated for each EU/EEA country (in DID) from 2015 to 2022 and changes in antibiotic consumption between 2019 and 2022 were analysed to evaluate the community consumption throughout the pandemic. To investigate any differences between low- and high-consuming countries, the correlation between the overall antibiotic consumption in 2021 and the change in antibiotic consumption between 2021 and 2022 was assessed. The quarterly and yearly mean antibiotic consumptions within the EU/EEA were calculated by weighting for the population size of all countries reporting data for the considered quarter or year. Antibiotic subclasses substantially contributing to the overall consumption (J01) were identified, and the evolution in these subclasses, as well as in the overall antibiotic consumption (J01), was further investigated using non-linear changepoint mixed models, as described by Bruyndonckx et al. [9]. To assess the seasonal variation in antibiotic consumption, the changepoint models were applied to all available quarterly data (16 countries, Supplementary table S1). Additionally, to estimate the actual magnitude of the changes, an analysis was performed including yearly data from all 28 EU/EEA countries, if available. Models containing two changepoints were fitted and reduced if necessary. Since it was previously shown that the decrease in antibiotic use between 2019 and 2020 was abrupt, only models with a change in intercept at the first changepoint were included in the analysis [3]. The most elaborate model included: (i) two changes in intercept, indicating abrupt decreases or increases in antibiotic consumption; (ii) two changes in slope, indicating gradual decreasing or increasing trends in antibiotic consumption; and (iii) two changes in amplitude, indicating decreases or increases in seasonal variation. Note that the estimates obtained from the non-linear changepoint mixed model are not weighted by population size. Further details on the model structures and model fitting can be found in the Supplementary materials.

Results

In the European countries examined, a decrease in overall antibiotic consumption (J01) from 18.36 DID in 2019 to 14.95 DID in 2020 was found (-18.57%), and has been described previously in detail by Vermeulen et al., together with the observed changes in the consumption of specific antibiotic subclasses [3]. Between 2020 and 2021, the overall antibiotic consumption remained rather stable, as well as the consumption of the antibiotic subclasses. Between 2021 and 2022, an increase in overall antibiotic consumption from 14.98 DID to 18.04 DID was found (+20.43%). The antibiotic subclasses mainly contributing to the overall antibiotic consumption were penicillins (J01C), macrolides, lincosamides and streptogramins (J01F), and other β-lactam antibacterials (J01D). Table 1 shows the overall antibiotic consumption (J01) and the consumption of all antibiotic subclasses in Europe, from 2019 to 2022, as well as the observed changes in this period. Figure 1 shows the yearly and quarterly evolution in overall antibiotic consumption, and in the consumption of the most frequently used antibiotic subclasses.

Between 2021 and 2022, an increase in overall antibiotic consumption (J01) was observed for every EU/EEA country. The largest relative increases were in Malta, Greece and Slovakia. The smallest relative increases were in Denmark, Romania and Bulgaria. Although borderline, no significant correlation was found between the overall antibiotic consumption in 2021 and the size of the increase from 2021 to 2022 (corr.=0.37; $p=0.06$). Overall antibiotic consumption (J01) was higher in 2022 than in 2019, i.e. before the pandemic, for Bulgaria, Croatia, Estonia, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, Norway, Poland, Romania and Slovakia. Supplementary table S2 shows the overall antibiotic consumption (J01) from 2019 to 2022 for each individual EU/EEA country, highlighting considerable differences in consumption across countries. Although overall antibiotic consumption (J01) rose again in each EU/EEA country between 2021 and 2022, decreases in the use of certain antibiotic subclasses were observed in several countries. Supplementary table S3 provides an overview of the changes in antibiotic consumption between 2021 and 2022 for each antibiotic subclass and country.

Changepoint analysis

Overall antibiotic consumption (J01)

The overall antibiotic consumption in the EU/EEA in 2015 was estimated at 17.64 DID and significantly decreased with 0.17 DID per year until the first changepoint between 2019 and 2020, where antibiotic consumption abruptly decreased with 2.77 DID. At the second changepoint, between 2021 and 2022, antibiotic consumption increased again with 3.33 DID. The overall antibiotic consumption in 2015 in EU/EEA countries reporting quarterly data was estimated at 16.58 DID and significantly decreased over time with 0.09 DID per quarter until the first changepoint between the first and second quarters of 2020, where antibiotic consumption abruptly decreased with 4.56 DID. Afterwards, antibiotic consumption gradually increased again with 0.55 DID per quarter. The analysis showed significant seasonality, with an amplitude of 2.72 DID, which decreased with 1.64 DID at the first changepoint between the first and

Table 1 Population-weighted mean of the overall (J01) and antibiotic subclass consumption and corresponding changes, expressed in DDD per 1000 inhabitants per day in the EU/EEA community sector, 2019–2022

	2019	2020	2021	2022	2019 vs. 2020		2020 vs. 2021		2021 vs. 2022	
					Absolute change	Relative change	Absolute change	Relative change	Absolute change	Relative change
Overall consumption of antibiotic (J01)	18.36	14.95	14.98	18.04	-3.41	-18.57%	+0.03	+0.20%	+3.06	+20.43%
Penicillins (J01C)	8.36	6.44	6.52	8.13	-1.92	-22.97%	+0.08	+1.24%	+1.61	+24.69%
Macrolides, lincosamides & streptogramins (J01F)	2.87	2.37	2.38	3.21	-0.50	-17.42%	+0.01	+0.42%	+0.83	+34.87%
Other beta-lactam antibacterials (J01D)	2.25	1.67	1.59	2.08	-0.58	-25.78%	-0.08	-4.79%	+0.49	+30.82%
Tetracyclines (J01A)	1.75	1.63	1.67	1.64	-0.12	-6.86%	+0.04	+2.45%	-0.03	-1.80%
Quinolone antibacterials (J01M)	1.41	1.20	1.16	1.30	-0.21	-14.89%	-0.04	-3.33%	+0.14	+12.07%
Other antibacterials (J01X)	1.03	1.00	1.03	1.00	-0.03	-2.91%	+0.03	+3.00%	-0.03	-2.91%
Sulfonamides and trimethoprim (J01E)	0.55	0.51	0.51	0.57	-0.04	-7.27%	0.00	0.00%	+0.06	+11.76%
Low consumption antibacterials (J01B, J01G and J01R)	0.14	0.13	0.12	0.11	-0.01	-7.14%	-0.01	-7.69%	-0.01	-8.33%

EU/EEA : European Union/European Economic area; vs.: versus; No data were available for Czechia in 2019 and 2020; and for Sweden in 2022.

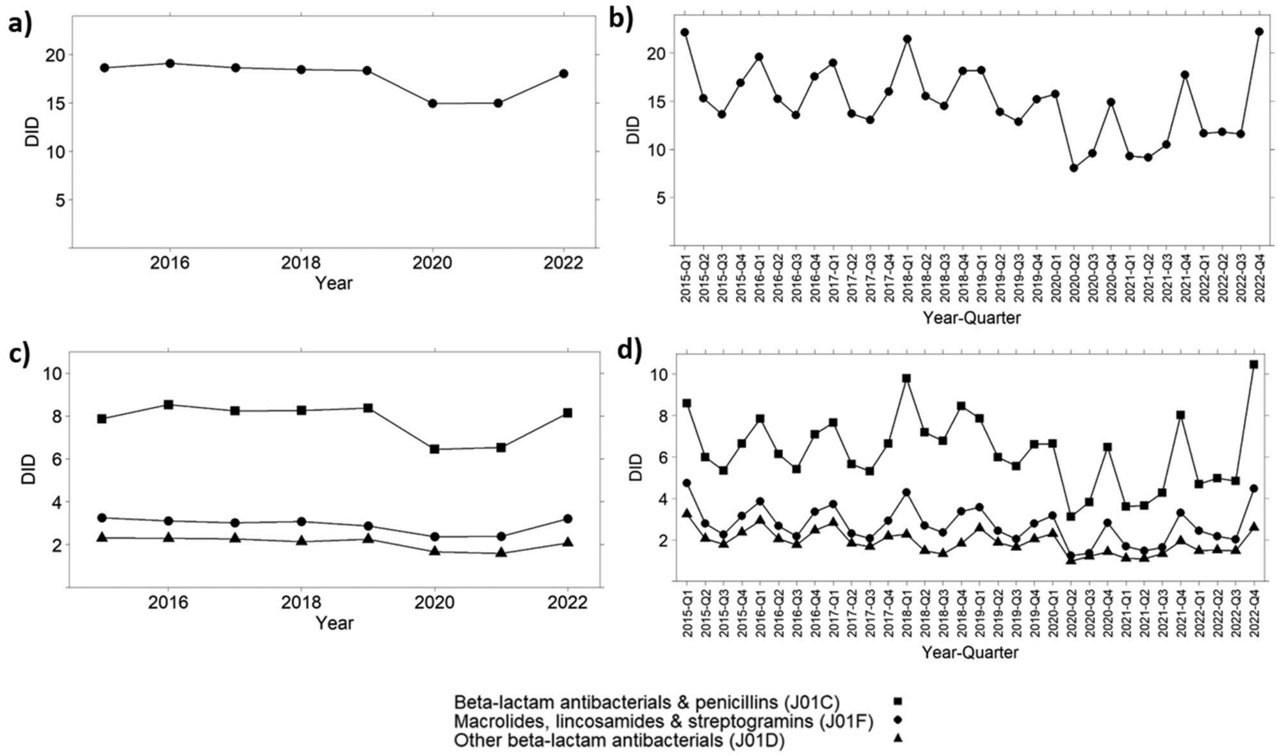

Fig. 1 **(a)** Annual evolution in the population-weighted overall antibiotic consumption (J01) in all 28 EU/EEA countries (Supplementary table S1). **(b)** Seasonal evolution in the population-weighted overall antibiotic consumption (J01) in 16 countries reporting quarterly data (Supplementary table S1). **(c)** Annual evolution in the population-weighted consumption of penicillins (J01C), macrolides, lincosamides and streptogramins (J01F) and other beta-lactam antibacterials (J01D) in all 28 EU/EEA countries (Supplementary table S1). **(d)** Seasonal evolution in the population-weighted consumption of penicillins (J01C), macrolides, lincosamides and streptogramins (J01F) and other beta-lactam antibacterials (J01D) in 16 countries reporting quarterly data (Supplementary table S1). **DID**: defined daily doses (DDD) per 1000 inhabitants per day

second quarters of 2020 and did not significantly change afterwards.

Consumption of penicillins (J01C)

The consumption of penicillins in the EU/EEA in 2015 was estimated at 7.39 DID and did not significantly change until the first changepoint between 2019 and 2020, where the consumption of penicillins abruptly decreased with 1.62 DID. At the second changepoint, between 2021 and 2022, penicillin consumption increased again with 1.61 DID. The consumption of penicillins in 2015 in EU/EEA countries reporting quarterly data was estimated at 7.16 DID and did not significantly change over time until the first changepoint between the first and second quarters of 2020, where penicillin consumption decreased with 2.67 DID. Afterwards, penicillin consumption gradually increased again with 0.28 DID per quarter. The analysis showed significant seasonality, with an amplitude of 1.21 DID, which decreased with 0.89 DID at the first changepoint between the first and second quarters of 2020 and did not significantly change afterwards.

Consumption of macrolides, lincosamides & streptogramins (J01F)

The consumption of macrolides, lincosamides and streptogramins in the EU/EEA in 2015 was estimated at 3.04 DID and significantly decreased with 0.06 DID per year until the first changepoint between 2019 and 2020, where the consumption abruptly decreased with 0.44 DID. At the second changepoint, between 2021 and 2022, the consumption increased again with 0.88 DID. The consumption of macrolides, lincosamides and streptogramins in 2015 in EU/EEA countries reporting quarterly data was estimated at 2.89 DID and significantly decreased over time with 0.02 DID per quarter until the first changepoint between the first and second quarters of 2020, where the consumption decreased with 0.89 DID. Afterwards, the consumption gradually increased again with 0.12 DID per quarter. The analysis showed significant seasonality, with an amplitude of 0.69 DID. No significant changes in seasonality were found.

Consumption of other beta-lactam antibacterials (J01D)

The consumption other beta-lactam antibacterials in the EU/EEA in 2015 was estimated at 2.09 DID and did not significantly change until the first changepoint between 2019 and 2020, where the consumption abruptly decreased with 0.49 DID. At the second changepoint, between 2021 and 2022, the consumption increased again with 0.46 DID. The consumption of other beta-lactam antibacterials in 2015 in EU/EEA countries reporting quarterly data was estimated at 1.62 DID and did not significantly change over time until the first changepoint between the first and second quarters of 2020, where the consumption decreased with 0.32 DID. The analysis showed significant seasonality, with an amplitude of 0.35 DID, which decreased with 0.24 DID at the first changepoint between the first and second quarters of 2020 and did not significantly change afterwards.

The estimated parameters for the changepoint models are given in Table 2 and describe the evolution and changes in the overall antibiotic consumption and the consumption of the most important antibiotic subclasses in the EU/EEA community.

Discussion

Our results align with previously reported levels and changes in antibiotic consumption in the EU/EEA [2–4, 10]. Between 2021 and 2022 a rebound in antibiotic consumption was observed, with levels exceeding pre-pandemic consumption in several countries. These findings might indicate decreased or at least altered efforts in antimicrobial stewardship (AMS) compared to the pre-pandemic period, as suggested by several studies [11, 12]. This underlines the importance of continued AMS within the EU and the development of AMS strategies that can be deployed and sustained during future pandemics. Although a strong association between the overall antibiotic consumption in 2019 and the size of the decrease between 2019 and 2020 was previously observed, no significant correlation was found between the overall antibiotic consumption in 2021 and the size of the increase between 2021 and 2022 [2].

The changepoint analysis on the quarterly data revealed an abrupt decrease in overall antibiotic consumption, penicillin consumption (J01C) and the consumption of macrolides, lincosamides and streptogramins (J01F) between the first and second quarters of 2020, and a gradual increase afterwards. These results indicate a difference in the immediate and long-term impact of the COVID-19 pandemic on antibiotic use in Europe, as was also observed by Domingues et al., who analysed monthly antibiotic consumption data for Portugal [13]. The abrupt decrease in antibiotic use at the beginning of the pandemic could be attributed to patients' hesitancy to seek medical care for mild symptoms, increased pressure on the health care system [14, 15], and reduced disease transmission observed during the COVID-19 pandemic due to non-pharmaceutical interventions [16]. Afterwards, the transmission of non-COVID communicable diseases increased gradually, consistent with the stepwise lifting of non-pharmaceutical interventions throughout the pandemic in Europe [16], which might have resulted in the gradual increase in antibiotic use. Additionally, as the COVID-19 pandemic progressed, patients might have become more inclined to seek medical care due to the worsening of their symptoms, increased confidence to visit their general practitioner safely, or decreased pressure on the health care system, again leading to a gradual increase in antibiotic use. No long-term effect, i.e. gradual increase, was found in the consumption of other beta-lactam antibacterials (J01D). However, since the consumption of other beta-lactam antibacterials increased with only 0.41 DID between 2020 and 2022, the observed changes might just be too small to be detected by the model. It has to be noted that the increase in antibiotic use during the late pandemic-period coincided with the mass COVID-19 vaccination program in the EU/EEA. Since COVID-19 vaccination is shown to be associated with reduced antibiotic prescribing in older outpatients, future decreases in the vaccination rate in this age group could result in an even further increase in antibiotic use [17, 18].

The analysis of quarterly data further showed a significant decrease in the seasonality of overall antibiotic use, penicillin use (J01C) and the use of other beta-lactam antibacterials (J01D), while an increase in seasonality during the late COVID-19 pandemic remained absent. A decrease in seasonal variation during the COVID-19 pandemic has been observed in previous studies [3, 13], and the fact that no significant rebound in seasonal variation was observed might indicate inappropriate use of antibiotics in the treatment of viral infections during the pre-pandemic period. Several studies have shown an association between seasonal respiratory virus activity and antibiotic prescriptions in the community during the COVID-19 pandemic [19–21]. This suggests that, in normal, non-pandemic periods, a significant share of antibiotics may be inappropriately prescribed for viral infections. These results provide useful insights for future AMS programs and indicate that reducing inappropriate use of antibiotics for seasonal viral infections, can significantly improve antibiotic prescribing quality.

Strengths and limitations

To the best of our knowledge, this is the first study that investigated the impact of the COVID-19 pandemic on antibiotic use and its seasonality in Europe, including data from the late-pandemic period (2022). The evolution of antibiotic use in the post-pandemic period, however, remains to be evaluated when more recent data become available. Although the changepoint mixed modelling framework is a valuable tool to investigate the significance and timing of the changes in antibiotic use,

Table 2 Overall community consumption of antibiotics (J01) and antibiotic subclasses in the EU/EEA, 2015–2022: parameter estimates (95% credible intervals (CrI)) based on changepoint analyses of quarterly data (16 EU/EEA countries, Supplementary table S1) and yearly data (28 EU/EEA countries, Supplementary table S1)

	Overall antibiotic consumption (J01)		**Penicillins (J01C)**		**Macrolides, lincosamides & streptogramins (J01F)**		**Other beta-lactam antibacterials (J01D)**	
	Quarterly data	**Yearly data**	**Quarterly data**	**Yearly data**	**Quarterly data**	**Yearly data**	**Quarterly data**	**Yearly data**
Intercept	16.58 (14.35 ; 18.69)*	17.64 (15.61 ; 19.66)*	7.16 (5.93 ; 8.36)*	7.39 (6.25 ; 8.48)*	2.89 (2.33 ; 3.42)*	3.04 (2.45 ; 3.59)*	1.62 (1.06 ; 2.20)*	2.09 (1.43 ; 2.78)*
Change in intercept	**CP1**: -4.56 (-5.33 ; -3.82)* **CP2**: 2.72 (-35.12 ; 40.24)	**CP1**: -2.77 (-3.60 ; -1.95)* **CP2**: 3.33 (2.72 ; 3.95)*	**CP1**: -2.67 (-3.16 ; -2.19)* **CP2**: 1.57 (-34.87 ; 37.67)	**CP1**: -1.62 (-1.97 ; -1.28)* **CP2**: 1.61 (1.34 ; 1.88)*	**CP1**: -0.89 (-1.13 ; -0.65)* **CP2**: 0.61 (-29.67 ; 30.33)	**CP1**: -0.44 (-0.75 ; -0.12)* **CP2**: 0.88 (0.60 ; 1.17)*	**CP1**: -0.32 (-0.47 ; -0.18)* **CP2**: 0.50 (-22.74 ; 24.22)	**CP1**: -0.49 (-0.74 ; -0.26)* **CP2**: 0.46 (0.28 ; 0.63)*
Slope	-0.09 (-0.14 ; -0.04)*	-0.17 (-0.32 ; -0.01)*	-0.02 (-0.04 ; 0.003)	-0.01 (-0.08 ; 0.06)	-0.02 (-0.04 ; -0.01)*	-0.06 (-0.10 ; -0.02)*	-0.01 (-0.02 ; -0.01)*	-0.01 (-0.06 ; 0.03)
Change in slope	**CP1**: 0.55 (0.45 ; 0.65)* **CP2**: 0.99 (-56.48 ; 58.07)	NI	**CP1**: 0.28 (0.22 ; 0.34)* **CP2**: 0.64 (-56.63 ; 57.90)	NI	**CP1**: 0.12 (0.08 ; 0.16)* **CP2**: -0.04 (-56.65 ; 56.27)	NI	NI	NI
Seasonality	2.72 (2.08 ; 3.37)*	NI	1.21 (0.91 ; 1.50)*	NI	0.69 (0.47 ; 0.91)*	NI	0.35 (0.18 ; 0.52)*	NI
Change in seasonality	**CP1**: -1.64 (-2.34 ; -0.91)* **CP2**: 1.42 (-54.25 ; 57.44)	NI	**CP1**: -0.89 (-1.27 ; -0.49)* **CP2**: 0.61 (-55.4 ; 57.09)	NI	NI	NI	**CP1**: -0.24 (-0.35 ; -0.14)* **CP2**: 0.35 (-57.66 ; 57.25)	NI
Changepoint	**CP1**: Between 1st and 2nd quarter of 2020* **CP2**: Between 3rd and 4th quarter of 2022	**CP1**: Between 2019 and 2020* **CP2**: Between 2021 and 2022*	**CP1**: Between 1st and 2nd quarter of 2020* **CP2**: Between 3rd and 4th quarter of 2022	**CP1**: Between 2019 and 2020* **CP2**: Between 2021 and 2022*	**CP1**: Between 1st and 2nd quarter of 2020* **CP2**: Between 3rd and 4th quarter of 2022	**CP1**: Between 2019 and 2020* **CP2**: Between 2021 and 2022*	**CP1**: Between 1st and 2nd quarter of 2020* **CP2**: Between 3rd and 4th quarter of 2022	**CP1**: Between 2019 and 2020* **CP2**: Between 2021 and 2022*

CP: changepoint, **NI**: not included, **Intercept**: consumption in 2015; **Change in intercept**: sudden increase/decrease in consumption at the changepoint; **Slope**: gradual increase/decrease in consumption per quarter/year before the first change-point; **Change in slope**: difference in slope after versus before the changepoint; **Seasonality**: amplitude describing the magnitude of the upward winter and downward summer peak; **Change in seasonality**: increase/decrease in the amplitude describing the magnitude of the upward winter and downward summer peak; **Changepoint**: timing of the changepoint; *: significant at 5% confidence level. Note that the estimates from the non-linear changepoint mixed model are not weighted by population size.

it should be noted that the obtained estimates are not weighted for population size. We therefore also reported the population-weighted mean estimates of antibiotic use in the EU/EEA and emphasise that the primary objective of the changepoint analysis is to investigate the timing and significance of any observed changes. Further, only 16 out of 28 countries reported quarterly data, potentially biasing the estimated seasonality (Supplementary table S1). We therefore believe reporting quarterly data should be encouraged to improve the accuracy of future studies.

Abbreviations

AMS	Antimicrobial stewardship
ATC code	Anatomical Therapeutic Chemical code
DDD	Defined Daily Doses
DID	DDDs per 1000 inhabitants per day
ECDC	European Centre for Disease Prevention and Control
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
EU/EEA	European Union/European Economic Area
J01C	Penicillins
J01D	Other β-lactam antibacterials
J01F	Macrolides, lincosamides and streptogramins
TESSy	The European Surveillance System
95%CrI	95% credible interval

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13690-024-01427-w.

Supplementary Material 1

Acknowledgements

We would like to thank Vivian Leung and Dragos Constantinescu for providing the ESAC-Net data. 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.

Author contributions

H.V., B.C. and N.H. contributed to the conception of the work. H.V. conducted the data acquisition, statistical analysis, interpreted the results and drafted the manuscript. L.C., B.C. and N.H. substantively revised the work. All authors read and approved the final manuscript.

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.

Data availability

The data that support the findings of this study are available from ESAC-Net but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of ESAC-Net.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Transparency declarations

The views and opinions of the authors expressed herein do not necessarily state or reflect those of ECDC. The accuracy of the authors' statistical analysis and the findings they report are not the responsibility of ECDC. ECDC is not responsible for conclusions or opinions drawn from the data provided. ECDC is not responsible for the correctness of the data and for data management, data merging and data collation after provision of the data. ECDC shall not be held liable for improper or incorrect use of the data.

Received: 6 September 2024 / Accepted: 17 October 2024
Published online: 31 October 2024

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