

# Antimicrobial consumption in the EU/EEA

Annual epidemiological report for 2018

### **Key facts**

- In 2018, the average total consumption (community and hospital sector combined) of antibacterials for systemic use (ATC group J01) in the EU/EEA was 20.1 DDD per 1 000 inhabitants per day (country range: 9.7–34.0). During the period 2009–2018, no statistically significant change was observed for the EU/EEA overall. However, statistically significant decreasing trends were observed for 11 countries. Statistically significant increasing trends were observed for four countries.
- The average consumption of antivirals for systemic use (ATC group J05) in both sectors (community and hospital sector combined) was 2.2 DDD per 1 000 inhabitants per day (country range: 0.51–6.78).
- Twenty-eight countries 26 EU Member States and two EEA countries (Iceland and Norway) reported data on antimicrobial consumption for 2018. Twenty-four countries reported both community and hospital consumption, three countries reported only community consumption, and one country reported total consumption for both sectors but without differentiating between them.
- Antimicrobial consumption is expressed as the number of defined daily doses (DDDs) per 1 000 inhabitants per day. The Anatomical Therapeutic Chemical (ATC) DDD Index 2019 was used for the analysis of 2018 data as well as of historical data in order to assess 10-year trends.
- The most recent data on antimicrobial consumption are available from the public <u>ESAC-Net interactive</u> <u>database</u> (data for 1997–2018) on the ECDC website.

#### **Community (primary care sector)**

- In the community, the average consumption of antibacterials for systemic use (ATC group J01) was 18.4 DDD per 1 000 inhabitants per day (country range: 8.9–32.4). During the period 2009–2018, no statistically significant change was observed for the EU/EEA overall. However, statistically decreasing trends were observed for nine countries (Austria, Belgium, Denmark, Finland, Italy, Luxembourg, the Netherlands, Portugal and Sweden). Statistically significant increasing trends were observed for four countries (Bulgaria, Ireland, Latvia and Poland).
- The average ratio of consumption of broad-spectrum penicillins, cephalosporins, macrolides (except erythromycin) and fluoroquinolones to the consumption of narrow-spectrum penicillins, cephalosporins and macrolides (i.e. erythromycin) in the community was 2.9 (country range: 0.1–24.0). During the period 2009–2018, statistically significant increasing trends were observed for the EU/EEA overall and for seven countries specifically. However, statistically significant decreasing trends were observed for eight countries.
- The average consumption of antimycotics and antifungals for systemic use (ATC groups J02 and D01B) in the community was 1.0 DDD per 1 000 inhabitants per day (country range: 0.39–3.0).

Suggested citation: European Centre for Disease Prevention and Control. Antimicrobial consumption in the EU/EEA, annual epidemiological report for 2018. Stockholm: ECDC; 2019.

Stockholm, November 2019

#### **Hospital sector**

- In the hospital sector, the average consumption of antibacterials for systemic use (ATC group J01) was 1.8 DDD per 1 000 inhabitants per day (country range: 0.8–2.5). During the period 2009–2018, no statistically significant change was observed for the EU/EEA overall. However, statistically significant decreasing trends were observed for five countries (Belgium, Finland, Latvia, Luxembourg and Norway), and statistically significant increasing trends were observed for seven countries (Bulgaria, Croatia, Denmark, Ireland, Malta, Portugal and Sweden).
- The average consumption of carbapenems in the hospital sector was 0.04 DDD per 1 000 inhabitants per day (country range: 0.01–0.12); this average did not increase significantly between 2009 and 2018. Statistically significant increasing trends were observed for six countries (Bulgaria, Croatia, Denmark, Estonia, Hungary and Malta), and statistically significant decreasing trends were observed for two countries (Portugal and Norway) during the same period.
- The average consumption of polymyxins in the hospital sector was 0.01 DDD per 1 000 inhabitants per day (country range: <0.001–0.07) and increased significantly between 2009 and 2018. Statistically significant increasing trends were observed for nine countries (Bulgaria, Denmark, Estonia, Hungary, Latvia, Norway, Portugal, Slovenia, Portugal and Sweden), and statistically significant decreasing trends were reported for one country (Ireland).
- The average proportion of glycopeptides, third- and fourth-generation cephalosporins, monobactams, carbapenems, fluoroquinolones, polymyxins, piperacillin and enzyme inhibitor, linezolid, tedizolid and daptomycin consumption out of total consumption of antibacterials for systemic use in the hospital sector was 32.5% (country range: 17-58%). During the period 2009–2018, statistically significant increasing trends were observed for the EU/EEA overall and seven countries specifically, whereas no country showed a statistically significant decreasing trend.
- The average consumption of antimycotics and antifungals for systemic use (ATC groups J02 and D01B) in the hospital sector was 0.16 DDD per 1 000 inhabitants per day (country range: 0.03–0.21).

#### **Methods**

This report is based on data for 2018 retrieved from The European Surveillance System (a system for the collection, storage, analysis and dissemination of data on communicable diseases) on 18 October 2019. For a detailed description of methods used to produce this report, please refer to the methods chapter in the introduction to the ECDC annual epidemiological report [1].

An overview of national surveillance systems is available online [2]. A subset of the data used for this report is available through ECDC's online antimicrobial consumption database (ESAC-Net) [3].

This surveillance report is based on antimicrobial consumption data reported by 26 EU Member States and two EEA countries (Iceland and Norway). The data sources for antimicrobial consumption were the same as in the previous report on ESAC-Net data. For the United Kingdom, Northern Ireland reported data from the hospital sector for the first time.

Antimicrobial consumption data are collected using the Anatomical Therapeutic Chemical (ATC) classification system and defined daily dose (DDD) methodology developed by the WHO Collaborating Centre for Drug Statistics Methodology (Oslo, Norway). For the analysis, DDDs listed in the ATC Index for 2019 were used [4]. One DDD is the assumed average maintenance dose per day for a drug used in its main indication in adults. It is a technical unit of measurement, not a standard for appropriate use. Application of the ATC/DDD methodology makes it possible to aggregate different brands of medicines with different pack sizes and strengths into units of measurement of active substances. It represents a standard in performing valid and reliable cross-national or longitudinal studies of antimicrobial consumption. DDD values of some medicines may change over time because of alterations in the main indication, or regulatory amendments for the recommended or prescribed daily dose. In case of such changes, all historical data require retrospective adjustments to the latest DDD/ATC index [4].

<sup>\*</sup> Important note: data were updated using the ATC/DDD Index 2019, which included several DDD alterations. Therefore, data reported in this report should not be compared with data previously reported by ECDC; readers should instead refer to the most current report or the ESAC-Net interactive database for the most recent data on antimicrobial consumption and trends in EU/EEA countries.

In 2019, the WHO Collaborating Centre for Drug Statistics Methodology changed the DDDs for nine antimicrobials and routes of administration: ampicillin (from 2g to 6g), oral amoxicillin (from 1g to 1.5g), parenteral amoxicillin (from 1g to 3g), oral amoxicillin with beta-lactamase inhibitor (from 1g to 1.5g), parenteral temocillin (from 2g to 4g), cefepime (from 2g to 4.5g), meropenem (from 2g to 3g), parenteral ciprofloxacin (from 0.5g to 0.8g), and parenteral colistin (from 3g to 9g). Consequently, historical ESAC-Net data on antimicrobial consumption since 1997 were recalculated accordingly. Therefore, historical antimicrobial consumption data in this report may differ from previously published data.

Additionally, the European Surveillance System database allows for correction and re-uploading of historical data by reporting countries. Therefore, the latest published reports supersede previous reports and reflect the most recent available data.

There are three major categories of antimicrobials under surveillance:

- a) antibacterials for systemic use (ATC group J01)
- b) antimycotics and antifungals for systemic use (ATC groups J02 & D01B)
- c) antivirals for systemic use (ATC group J05).

Due to the structure of the ATC classification, some antibacterials under surveillance are classified in ATC groups other than J01. For example, vancomycin and fidaxomicin for oral administration are classified as intestinal anti-infectives in ATC group A07A, and are used against *Clostridioides* (*Clostridium*) *difficile* infections. Metronidazole, which may also be orally administered against *C. difficile*, is classified as an agent against amoebiasis and other protozoal diseases in ATC group P01A. Rifampicin is classified as a drug for the treatment of tuberculosis (ATC group J04A). In clinical practice, rifampicin is also used for *Haemophilus influenzae* infections or in combination with other antibacterials to treat meticillin-resistant *Staphylococcus aureus* (MRSA) infections, brucellosis, Legionnaires' disease and serious staphylococcal infections.

Consumption data were collected for the community (primary care) sector and the hospital (secondary care and tertiary care) sector as a detailed list of all available antimicrobial products (register) and the annual number of packages consumed, or, if unavailable, as the number of DDD per ATC substance and route of administration. Consumption of antibacterials, antimycotics and antifungals for systemic use are presented separately for the community and the hospital sector, while the data on antivirals for systemic use for both the community and the hospital sector are combined.

The indicator 'defined daily doses (DDD) per 1 000 inhabitants per day' is used to report antibiotic consumption in the community (i.e. outside hospitals) [4,5] and in the hospital sector. It provides a rough estimate of the proportion of the population treated daily with antimicrobials.

Defined Daily Doses per 1 000 inhabitants per day was applied in this report as an indicator for antimicrobial consumption. Although the number of DDDs per 100 occupied bed-days has been recommended for presenting hospital consumption [4,6], the DDDs per 1 000 inhabitants per day was chosen for both the community and the hospital sector. This is because uniformly defined denominator data on the total number of occupied bed-days are currently unavailable for all EU/EEA countries. In addition, presenting data with the same denominator enables cross-sectoral comparison. The DDD per 1 000 inhabitants per day has been selected as the primary harmonised outcome indicator by ECDC, the European Food Safety Authority (EFSA) and the European Medicines Agency (EMA) to describe total antimicrobial consumption in humans in both the community and hospital sectors [7].

Likewise, the pattern of antimicrobial consumption was selected as a secondary harmonised outcome indicator after agreement between ECDC, EFSA and EMA. For the community, the agreed indicator is the ratio of consumption of broad-spectrum penicillins, cephalosporins, macrolides (except erythromycin) and fluoroquinolones to the consumption of narrow-spectrum penicillins, cephalosporins and erythromycin. For the hospital sector, the agreed indicator is the proportion of glycopeptides, 3rd- and 4th-generation cephalosporins, monobactams, carbapenems, fluoroquinolones, polymyxins, piperacillin and enzyme inhibitor, linezolid, tedizolid and daptomycin out of the total hospital consumption of antibacterials for systemic use.

'Consensus-based quality indicators', published in 2007 by the European Surveillance of Antimicrobial Consumption (ESAC) project were additionally applied to describe antimicrobial consumption [8].

The number of packages has not been recommended as a relevant and valid indicator for benchmarking the pattern and trends in antibacterial consumption between countries [4,5,6]. This indicator may serve as a proxy only for the number of prescriptions at the national level, provided that one antibiotic package is prescribed per prescription encounter. Data on the number of packages per 1 000 inhabitants per day are not shown in this report.

#### **EU/EEA** population-weighted average

For each country, antimicrobial consumption expressed as DDD per 1 000 inhabitants per day is displayed in all tables and figures of the report as reported by the country to the European Surveillance System; missing data for a year are displayed as empty cells in the tables. Antimicrobial consumption displayed with the label 'EU/EEA' and presenting only 2018 data is based on the data reported for a year and a selected ATC group or subgroup. All EU/EEA means are population-weighted and calculated by multiplying DDD per 1 000 inhabitants per day for each country with the corresponding Eurostat population, and dividing the product by the total population of participating EU/EEA countries.

To assess whether the EU/EEA 10-year trend of consumption for ATC group J01 and subgroups (five-year trend for ATC J05) was statistically significant, linear regression was applied. Missing values for country specific univariate time series were imputed by one of the following interpolation methods: linear interpolation, Spline regression or weighted moving average algorithms (where the missing values are replaced by moving average values). The imputation allows for inclusion of the same number of EU/EEA countries for all the years in the trend analyses. Imputing missing values was performed using the R package 'imputeTS'.

In case a country only reported aggregated community and hospital sector data ('total care') for a specific year, the value was corrected using mean distribution between hospital and community sector obtained from the other years in the studied period. If the country had not reported separate community and hospital data for any of the years during the studied time period (e.g. for Iceland), the EU/EEA average proportions were used.

For Spain, the community consumption data reported for the years 2009-2015 were adjusted proportionally due to the change in reported data sources from 2016 onwards. Spain changed reporting from reimbursement data to sales data, which resulted in a substantial technical increase of antimicrobial consumption compared with previous years, as the reimbursement data included consumption without a prescription and other non-reimbursed courses.

To illustrate changes in rates in antimicrobial consumption over time, we calculated the compound annual growth rate (CAGR) of total antibiotic consumption by each country [9]. It displays the average annual change as a proportion (%) of the consumption in the starting year.

More details on the methods, collection, validation and reporting of European antimicrobial consumption data are available from the <u>ESAC-Net pages</u> on ECDC's website. They are also described in the <u>ESAC-Net surveillance</u> reports [10]. The most recent data on antimicrobial consumption are available from the public <u>ESAC-Net interactive</u> database (data for 1997–2018) on ECDC's website [3].

#### **Antimicrobial consumption**

All EU Member States (except Cyprus and the Czech Republic) and two EEA countries (Iceland and Norway) reported data on antimicrobial consumption for 2018. Twenty-two countries reported both community and hospital consumption, three countries (Austria, Germany and Iceland) reported only community consumption, and one Romania) reported total consumption in both sectors without differentiating between them. Nevertheless, data from Romania are shown together with community consumption from other countries because, on average, approximately 90% of the total consumption data of antibacterials for systemic use (ATC group J01) refer to consumption in the community. For both the community and the hospital sector, consumption data were mainly based on sales of antimicrobials in the country or a combination of sales and reimbursement data.

### Total consumption (community and hospital sector) of antibacterials for systemic use (ATC group J01)

### ECDC/EFSA/EMA primary indicator for total consumption of antibacterials for systemic use (ATC group 01) in humans

In 2018, the average total consumption (community and hospital sector combined) of antibacterials for systemic use (ATC group J01) in the EU/EEA was 20.1 DDD per 1 000 inhabitants per day, ranging from 9.7 in the Netherlands to 34.0 in Greece. During the period 2009–2018, no statistically significant change was observed for the EU/EEA overall. However, statistically significant decreasing trends were observed for 11 countries. Statistically significant increasing trends were observed for four countries (Table1).

Table 1. Total consumption (community and hospital sector) of antibacterials for systemic use (ATC group J01) in EU/EEA countries, 2009–2018 (expressed as DDD per 1 000 inhabitants per day)

Country	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Trends in antimicrobial consumption, 2009–2018	CAGR Compound annual growth rate (%)	Trend
Austria	13.6*	13.1*	12.7*	12.2*	14.2*	12.1*	12.1*	11.4*	11.9*	10.4*	and have	-2.9%	1
Belgium	23.9	24.9	25.4	25.6	24.2	24.0	24.4	24.2	22.8	22.3	- many	-0.8%	<b>↓</b>
Bulgaria	17.3	17.2	18.3	17.4	18.6	20.0	20.1	19.2	20.5	21.0		2.1%	1
Croatia	20.7	18.8	18.2	20.0	19.2	19.4	19.7	18.7	18.6	18.8	1	-1.1%	
Cyprus	29.2	26.3	26.9	25.1	23.9	22.2	26.6	28.4	28.9		San	-0.1%	
Czech Republic	16.6*	16.0*	16.5*	15.7*	16.9*	17.1*	17.4*				~~~	0.7%	
Denmark	16.7	17.5	18.3	17.4	17.5	17.1	17.5	17.0	16.2	15.6	-	-0.7%	
Estonia	11.2	11.4	12.4	12.2	12.0	11.9	12.1	12.0	11.6	11.8	1	0.6%	
Finland	19.6	19.7	21.5	20.6	19.6	19.1	18.1	17.4	15.7	15.5		-2.6%	1
France	26.2	25.0	25.1	25.7	25.9	24.9	25.6	25.6	24.7	25.3	1	-0.4%	
Germany	13.8*	13.4*	13.1*	13.7*	14.5*	13.4*	13.1*	12.8*	12.3*	11.9*	-	-1.6%	<b>↓</b>
Greece	37.6	35.6	33.4	29.9	29.8	31.0	33.2	33.1	34.2	34.0	-	-1.1%	
Hungary	15.0	14.8	14.9	14.1	14.5	15.2	15.8	14.4	14.6	14.8		-0.1%	
Iceland	17.2*	19.8	19.8	19.7	19.4	17.1*	17.6*	18.2*	18.8*	20.4*	7	4.6%	1
Ireland	19.0	19.0	20.8	21.0	21.6	21.0	23.0	22.0	20.9	22.7		2.0%	1
Italy	23.7*	24.9	25.1	24.6	25.2	24.5	24.5	24.0	20.9	21.4	- marine	-1.9%	<b>↓</b>
Latvia	11.5	12.6	12.9	12.9	13.3	12.6	13.1	12.9	13.9	13.3	June 1	1.6%	1
Lithuania	16.2	14.4	15.5	15.3	17.1	15.1	15.8	15.6	15.7	17.5	~~~	0.9%	
Luxembourg	25.7	25.1	25.2	25.0	25.0	23.2	23.5	22.9	22.6	22.2	and have	-1.6%	1
Malta	19.8	19.9	21.6	20.8	22.2	22.4	21.2	20.9	22.6	20.9	~~~	0.6%	
Netherlands	10.1*	10.9	11.0	10.9	10.5	10.3	10.4	10.1	9.8	9.7	1	-0.4%	1
Norway	16.3	16.8	17.5	17.9	17.2	16.9	16.8	16.2	15.7	15.3	-	-0.7%	
Poland	20.1*	18.0*	18.2*	19.9*	20.5*	21.2	24.1	22.0	25.4	24.4		3.6%	
Portugal	20.4	19.9	20.6	20.1	17.6	18.0	18.8	19.0	17.8	18.6	~	-1.0%	1
Romania	12.1		26.5	25.9	26.8	26.6	28.0	24.4	24.5	25.0		-0.8%	
Slovakia	23.0		21.4*	19.7	23.2	21.2	24.2	23.6	20.0	22.0	. ~~~	0.5%	
Slovenia	13.5	13.4	13.4	13.2	13.3	13.1	13.3	12.1	12.2	13.2	-	-0.3%	1
Spain	15.7 <sup>†</sup>	16.2†	16.6†	15.7 <sup>†</sup>	16.2†	17.1†	17.5†	27.5	26.8	26.0		N/A	
Sweden	15.1	15.2	15.4	15.3	14.2	14.0	13.5	13.2	12.8	12.4		-2.1%	1
United Kingdom	15.2*	16.5*	16.5*	17.7*	20.4	20.8	20.1	19.7	19.3	18.8	-	-1.6%	1
EU/EEA	20.6	19.7	20.9	21.0	21.5	21.1	21.5	20.7	20.2	20.1	V.	-0.3%	

All country data are shown as they are reported to the European Surveillance System.

EU/EEA refers to the corresponding population-weighted mean consumption based on reported antimicrobial consumption data of all 30 EU/EEA countries. Through imputation and other adjustments, the EU/EEA averages include the same number of EU/EEA countries for all years of the trend analyses (see the method chapter).

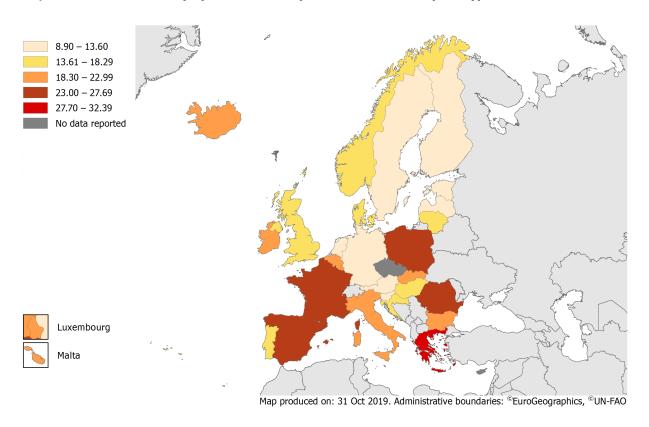
<sup>\* =</sup> countries reported only community data, † = Spain reported 2009-2015 reimbursement data and changed in 2016 to sales data; N/A = not applicable.

<sup>[</sup>light shaded cells] = linear regression was not applied for the highlighted cells, because of missing data, changes in the type of data or changes of sector for which data were reported (community versus total care data).

### Consumption of antibacterials for systemic use (ATC group J01) in the community

In 2018, the EU/EEA population-weighted mean consumption of antibacterials for systemic use in the community (i.e. outside hospitals) was 18.4 DDD per 1 000 inhabitants per day, ranging from 8.9 in the Netherlands to 32.4 in Greece (Figure 1).

Figure 1. Consumption of antibacterials for systemic use (ATC group J01) in the community in EU/EEA countries in 2018 (expressed as DDD per 1 000 inhabitants per day)



Romania provided total care data, i.e. including the hospital sector.

Consumption of major subgroups of antibacterials for systemic use (ATC group J01) in the community in 2018 is presented in Table 1 and Figure 3. As in previous years, penicillins (ATC group J01C) were the most frequently used antibacterials in all countries, ranging from 25% in Slovakia to 67% in Denmark of the total consumption in the community. The proportion of other antibacterial groups varied more widely between countries. For example, cephalosporins and other beta-lactams (ATC group J01D ranged from 0.2% in Denmark to 31% in Slovakia; macrolides, lincosamides and streptogramins (ATC group J01F) ranged from 5% in Sweden to 26% in Poland; and quinolone antibacterials (ATC group J01M), from 2% in Norway to 17% in Hungary.

Table 2. Consumption of antibacterials for systemic use (ATC group J01) by country and ATC group level 3 in the community in EU/EEA countries in 2018 (expressed as DDD per 1 000 inhabitants per day)

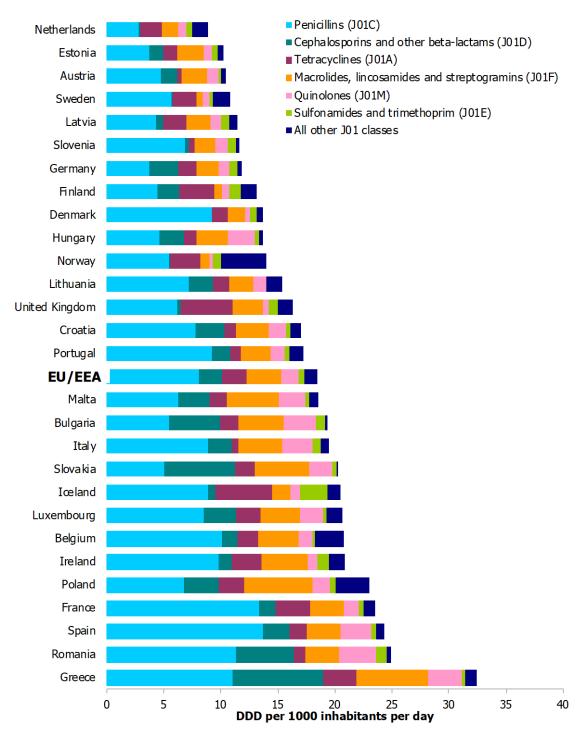
Country	Tetracyclines (J01A)	Beta- lactams, penicillins (J01C)	Other beta- lactam antibacterials (J01D)	Sulfonamides and trimethoprim (J01E)	Macrolides, lincosamides and streptogramins (J01F)	Quinolones (J01M)	Other antibacterials (J01X)	Sum (J01B, J01G, and J01R) *	Total (ATC group J01)
Austria	0.4	4.8	1.4	0.2	2.3	1.0	0.4	0.0	10.4
Belgium	1.9	10.1	1.3	0.2	3.6	1.2	2.5	0.0	20.8
Bulgaria	1.6	5.5	4.4	0.9	4.0	2.8	0.0	0.2	19.4
Croatia	1.0	7.8	2.5	0.5	2.8	1.5	0.8	0.0	17.0
Denmark	1.4	9.2	0.0	0.7	1.5	0.4	0.5	0.0	13.7
Estonia	1.2	3.7	1.2	0.4	2.3	0.8	0.6	0.0	10.2
Finland	3.1	4.4	1.9	1.0	0.7	0.6	1.5	0.0	13.2
France	3.1	13.3	1.4	0.4	2.9	1.3	0.4	0.7	23.6
Germany	1.6	3.7	2.5	0.6	1.9	1.0	0.5	0.0	11.9
Greece	2.9	11.1	7.9	0.3	6.3	2.9	0.9	0.1	32.4
Hungary	1.1	4.6	2.1	0.4	2.8	2.3	0.3	0.0	13.7
Iceland	5.0	8.9	0.6	2.5	1.6	0.8	1.1	0.0	20.4
Ireland	2.6	9.8	1.1	1.0	4.1	0.8	1.4	0.0	20.9
Italy	0.5	8.9	2.1	0.7	3.9	2.7	0.7	0.1	19.5
Latvia	2.0	4.4	0.6	0.7	2.0	0.9	0.7	0.0	11.4
Lithuania	1.4	7.2	2.1	0.0	2.2	1.1	1.4	0.1	15.4
Luxembourg	2.1	8.5	2.9	0.3	3.5	2.0	1.4	0.0	20.7
Malta	1.5	6.3	2.7	0.3	4.5	2.3	0.5	0.3	18.6
Netherlands	1.9	2.9	0.0	0.4	1.4	0.7	1.4	0.0	8.9
Norway	2.6	5.5	0.1	0.7	0.9	0.3	3.9	0.0	14.0
Poland	2.3	6.8	3.0	0.5	6.0	1.5	2.9	0.0	23.0
Portugal	0.9	9.2	1.6	0.3	2.7	1.2	1.2	0.0	17.2
Romania (a)	0.9	11.3	5.1	0.8	3.0	3.3	0.3	0.2	25.0
Slovakia	1.7	5.0	6.2	0.4	4.7	2.1	0.1	0.0	20.2
Slovenia	0.5	6.9	0.3	0.7	1.8	1.1	0.4	0.0	11.7
Spain	1.5	13.7	2.3	0.4	3.0	2.7	0.5	0.2	24.3
Sweden	2.2	5.7	0.1	0.3	0.5	0.6	1.5	0.0	10.8
United Kingdom	4.6	6.2	0.2	0.8	2.6	0.4	1.3	0.0	16.3
EU/EEA	2.1	8.1	2.0	0.6	3.0	1.5	1.0	0.1	18.4

<sup>(</sup>a) Romania provided total care data (i.e. including the hospital sector).

EU/EEA refers to the corresponding population-weighted mean consumption based on reported data for 2018.

<sup>\*</sup>J01B: Amphenicols; J01G: Aminoglycoside antibacterials; J01R: Combinations of antibacterials.

Figure 2. Consumption of antibacterials for systemic use (ATC group J01) by country and ATC group level 3 in the community in EU/EEA countries in 2018 (expressed as DDD per 1 000 inhabitants per day)



Romania provided total care data (i.e. including the hospital sector). EU/EEA refers to the corresponding population-weighted mean consumption based on the reported data for 2018.

The EU/EEA population-weighted mean consumption of antibacterials for systemic use decreased from 18.6 DDD per 1 000 inhabitants per day in 2009 to 18.4 in 2018, but there was no statistically significant trend for the tenyear period 2009–2018 (Table 2). However, statistically decreasing trends were observed for nine countries (Austria, Belgium, Denmark, Finland, Italy, Luxembourg, the Netherlands, Portugal and Sweden). Statistically significant increasing trends were observed for four countries (Bulgaria, Ireland, Latvia and Poland) for this period.

2017 Ţ 10.1 10.0 10.1 10.1 9.4 9.5 9.2 8.9 Netherlands 9.6 8.9 Estonia 9.7 9.8 10.7 10.3 10.3 10.2 10.5 10.4 9.9 10.2 0.6% Austria 13.6 13.1 12.7 12.2 14.2 12.1 12.1 11.4 11.9 10.4 -2.9% L 13.7 13.8 13.9 13.7 12.7 12.5 10.8 -2.6% Sweden 11.9 11.7 11.3 9.3 9.9 10.8 11.0 11.3 10.6 11.1 11.1 12.1 11.4 2.3% Slovenia 11.9 11.8 11.9 11.8 11.9 11.6 11.9 10.7 10.7 11.7 -0.2% 13.8 13.4 13.1 13.7 14.5 13.4 13.1 12.8 12.3 11.9 Germany -1.6% 1 16.6 17.0 18.6 18.0 16.9 16.6 15.8 15.0 13.6 13.2 -2.5% Finland 15.0 15.9 16.7 15.7 15.7 15.2 15.3 15.2 14.3 13.7 -1.0% 13.9 13.6 13.8 13.0 13.4 14.0 14.7 13.3 13.4 13.7 -0.1% 15.4 -0.7% Norway 14.9 16.1 16.5 15.8 15.5 15.4 14.9 14.4 14.0 Lithuania 16.2\* 14.4\* 15.5\* 13.3 15.1 13.1 13.6 13.5 13.6 15.4 2.5% 15.2 16.5 16.5 18.3 18.5 17.9 17.5 17.1 16.3 0.8% 19.4 17.2 16.5 18.3 17.6 17.8 18.0 17.1 16.8 17.0 -1.4% Croatia 19.1 18.6 18.7 16.1 17.3 17.5 -1.2% Portugal 19.2 16.6 16.4 17.2 EU/EEA 18.6 19.0 19.2 19.2 19.7 19.4 19.8 19.1 18.6 18.4 -0.1% 18.6 18.1 20.1 19.5 20.7 20.5 18.8 18.4 19.8 18.6 0.0% Bulgaria 15.9 15.8 17.0 16.1 17.3 18.6 18.8 17.6 18.9 19.4 2.2% ļ 23.7 23.0 22.5 22.4 19.5 -2.2% Italy 23.1 23.3 22.6 21.8 19.0 21.3 21.1 18.9 22.0 21.3 18.5 20.2 -0.8% Slovakia Iceland 17.2 19.8\* 19.8\* 19.4\* 17.1 17.6 18.2 18.8 20.4 4.6% ļ Luxembourg 23.8 23.2 23.3 23.1 23.1 21.6 21.8 21.4 20.9 20.7 -1.5% Ţ Belgium 22.2 23.1 23.6 23.9 22.6 22.4 22.8 22.5 21.1 20.8 -0.7% 17.8 17.4 19.2 19.5 20.0 19.5 21.3 20.4 19.4 20.9 1.8% Ireland Poland 20.1 18.0 18.2 19.9 20.5 19.9 22.8 20.7 23.8 23.0 1.5% France 24.4 23.2 23.4 24.0 24.1 23.1 23.8 23.9 23.0 23.6 -0.4% 15.7† 16.2† 15.7† 17.1† Spain 16.6† 16.2† 17.5† 25.6 25.0 24.3 N/A Romania 9.6 26.5\* 25.9\* 26.8\* 26.6\* 28.0\* 24.4\* 24.5\* 25.0 -0.8% 34.6 35.6\* 31.6 28.2 28.0 29.2 31.3 31.0 32.1 0.3% 29.2\* 26.3\* 26.9\* 25.1\* 23.9\* 22.2\* 26.6\* 28.4\* 28.9\* -0.1%

Table 3. Trends in consumption of antibacterials for systemic use (ATC group J01) in the community in EU/EEA countries, 2009–2018 (expressed as DDD per 1 000 inhabitants per day)

All country data are shown as they are reported to the European Surveillance System.

16.9

17.1

15.7

16.0

16.6

16.5

17.4

[light shaded cells] = linear regression was not applied for the highlighted cells, because of missing data, changes in the type of data or changes of sector for which data were reported (community versus total care data).

EU/EEA refers to the corresponding population-weighted mean consumption based on reported antimicrobial consumption data of all 30 EU/EEA countries. Through imputation and other adjustments, the EU/EEA averages include the same number of EU/EEA countries for all years of the trend analyses (see the method chapter).

There were statistically significant decreases in the EU/EEA average ten-year trends for consumption of subgroups of antibacterials in the community for tetracyclines (J01A), macrolides, lincosamides, streptogramins (J01F) and quionolones (J01M), while a statistically significant increase was seen for the subgroup of other antibacterials (J01X), which includes glycopeptides.

Trends in consumption of subgroups of antibacterials are available as downloadable tables D1, D2, D3, D4, D5, D6 and D7. The downloadable Tables and Figures are available on the ECDC website.

### ECDC/EFSA/EMA secondary indicator for consumption of antibacterials for systemic use (ATC group J01) in the community

The ratio of consumption of broad-spectrum penicillins, cephalosporins, macrolides (except erythromycin) and fluoroquinolones (J01(CR+DC+DD+(FA—FA01)+MA)) to the consumption of narrow-spectrum penicillins, cephalosporins and erythromycin (J01(CA+CE+CF+DB+FA01)) is presented in Figure 4. In 2018, the average ratio was 2.9 (country range: 0.1–24.0). During the period 2009–2018, statistically significant increasing trends was observed for the EU/EEA overall and 7 countries specifically. However, statistically decreasing trends were observed for eight countries.

0.7%

<sup>\* =</sup> total care data, † = Spain reported 2009-2015 reimbursement data and changed in 2016 to sales data; N/A = not applicable.

Table 4. The ratio of consumption of broad-spectrum penicillins, cephalosporins, macrolides (except erythromycin) and fluoroquinolones to the consumption of narrow-spectrum penicillins, cephalosporins and erythromycin expressed as DDD per 1 000 inhabitants per day in the community in EU/EEA countries, 2009–2018

Country	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Trends, 2009–2018	CAGR Compound annual growth rate (%)	Trend
Austria	4.3	4.2	4.1	4.4	4.4	4.4	4.4	4.2	4.2	3.9	-	-1.1%	
Belgium	2.9	2.3	2.4	2.4	2.0	2.2	2.2	2.2	2.2	2.1	my	-3.6%	1
Bulgaria	1.7	1.7	1.9	2.1	2.3	3.0	3.5	4.2	4.0	4.2		10.9%	1
Croatia	2.1	2.5	2.7	3.5	3.1	3.2	3.4	3.3	3.8	4.3		8.0%	1
Cyprus	4.4*	4.6*	4.8*	4.7*	5.5*	6.0*	6.7*	8.2*	8.8*			8.9%	1
Czech Republic	2.6	2.6	2.4	2.9	2.6	2.9	3.0					2.9%	
Denmark	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	1	1.4%	
Estonia	1.7	1.9	2.1	2.2	2.5	2.5	2.7	2.8	2.9	3.0		6.6%	1
Finland	0.5	0.5	0.5	0.5	0.4	0.4	0.4	0.4	0.4	0.3	-	-3.7%	1
France	1.8	1.8	1.7	1.7	1.5	1.4	1.3	1.2	1.1	1.0		-6.3%	1
Germany	1.8	1.9	2.1	1.9	1.9	1.9	2.0	1.9	1.7	1.7		-0.6%	
Greece	4.8	5.6*	5.3	4.5	4.4	7.0	4.8	3.8	4.9	4.9	~~~	0.3%	
Hungary	4.7	5.7	5.8	6.0	6.6	9.6	11.3	10.9	11.6	12.7		11.6%	1
Iceland	0.6	0.6*	0.7*	0.6*	0.8*	0.8	0.9	0.8	0.7	0.6		-0.5%	
Ireland	1.8	1.7	1.9	1.9	1.7	1.4	1.4	1.6	1.4	1.3		-2.9%	<b>1</b>
Italy	4.6	4.9	5.4	5.6	6.1	6.6	6.9	6.9	7.1	7.5		5.5%	1
Latvia	1.0	0.9	1.0	1.1	1.2	1.3	1.3	1.4	1.5	1.7		6.0%	1
Lithuania	0.7*	0.8*	0.8*	0.9	0.9	0.9	0.9	1.0	1.1	1.2		5.1%	1
Luxembourg	4.1	4.2	4.3	4.5	4.4	4.4	3.9	3.6	3.7	3.5	- marine	-1.9%	1
Malta	17.2	18.3	19.2	22.1	23.4	31.4	32.7	19.2	23.2	24.0		3.8%	
Netherlands	1.6	1.6	1.6	1.6	1.4	1.4	1.4	1.4	1.4	1.5	-	-0.6%	<b>1</b>
Norway	0.2	0.2	0.2	0.2	0.2	0.2	0.1	0.1	0.1	0.1		-3.9%	↓
Poland	2.6	2.7	3.2	2.3	2.4	2.5	2.6	2.6	2.9	3.2		2.6%	
Portugal	5.1	5.4	5.2	5.0	5.3	5.2	5.2	5.1	3.9	3.9	- marine	-2.9%	1
Romania	3.3		1.5*	1.8*	2.2*	2.2*	2.5*	3.1*	3.4*	3.9*	•	14.1%	1
Slovakia	4.2		5.1	4.9	5.3	5.6	6.6	6.5	6.6	8.0		6.7%	1
Slovenia	1.5	1.4	1.4	1.3	1.4	1.5	1.5	1.4	1.4	1.4	-	-0.2%	
Spain	3.2†	3.3†	3.2†	3.1†	3.1†	3.0†	3.1†	2.4	2.4	2.4		N/A	
Sweden	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2		0.7%	
United Kingdom	0.3	0.4	0.4	0.4	0.5	0.5	0.5	0.5	0.5	0.5		5.1%	1
EU/EEA	2.3	2.4	2.5	2.4	2.5	2.7	2.8	2.7	2.7	2.9	-	2.2%	1

All country data are shown as they are reported to the European Surveillance System.

[light shaded cells] = linear regression was not applied for the highlighted cells, because of missing data, changes in the type of data or changes of sector for which data were reported (community versus total care data).

EU/EEA refers to the corresponding population-weighted mean consumption based on reported antimicrobial consumption data of all 30 EU/EEA countries. Through imputation and other adjustments, the EU/EEA averages include the same number of EU/EEA countries for all years of the trend analyses (see the method chapter). ESAC quality indicators for consumption of antibacterials for systemic use (ATC group J01) in the community.

The relative consumption of beta-lactamase-sensitive penicillins, combinations of penicillins including beta-lactamase inhibitors, third- and fourth-generation cephalosporins and fluoroquinolones and the ratio of broad- to narrow-spectrum antibacterials, i.e. the 'consensus-based quality indicators,' are presented in Table D84and Figures D1, D2 and D4.

### Consumption of antibacterials from other ATC groups (A07A, P01A, J04A)

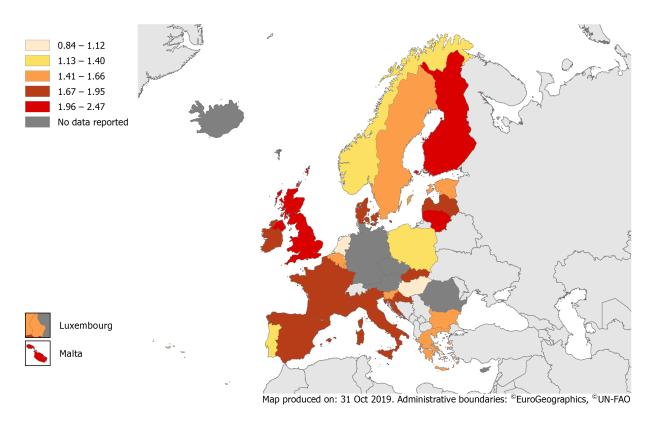
Eighteen countries reported community consumption of oral vancomycin (A07AA09) and fidaxomicin (A07AA12), while consumption of rifampicin (J04AB02) and oral and rectal metronidazole (P01AB01) were reported by 28 countries (Table D9).

<sup>\* =</sup> total care data, † = Spain reported 2009-2015 reimbursement data and changed in 2016 to sales data; N/A = not applicable.

### Consumption of antibacterials for systemic use (ATC group J01) in the hospital sector

In 2018, the EU/EEA population-weighted mean consumption of antibacterials for systemic use in the hospital sector was 1.8 DDD per 1 000 inhabitants per day, ranging from 0.8 in the Netherlands to 2.5 in United Kingdom (Figure 3).

Figure 3. Consumption of antibacterials for systemic use (ATC group J01) in the hospital sector in EU/EEA countries in 2018 (expressed as DDD per 1 000 inhabitants per day)



Finland: data include consumption in remote primary healthcare centres and nursing homes.

Portugal: data refer to public hospitals. Population was adjusted, based on hospital catchment area information provided by the country.

Consumption of major subgroups of antibacterials for systemic use (ATC group J01) in the hospital sector in 2018 is presented in Table 3 and Figures 3 and 4. Substantial variations were reported across countries: consumption of penicillins (ATC group J01C) ranged from 7% in Bulgaria to 60% in Sweden; consumption of cephalosporins and other beta-lactams (ATC group J01D, includes carbapenems) ranged from 7% in the United Kingdom to 56% in Bulgaria; consumption of macrolides, lincosamides and streptogramins (ATC group J01F) from 4% in Lithuania to 18% in Luxembourg, and consumption of quinolones (ATC group J01M) from 3% in Norway to 19% in Italy.

Table 5. Consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, by country and ATC group in EU/EEA countries in 2018 (expressed as DDD per 1 000 inhabitants per day)

Country	Tetracyclines (J01A)	Beta- lactams, penicillins (J01C)	Other beta- lactam antibacterials (J01D)	Sulfonamides and trimethoprim (J01E)	Macrolides, lincosamides and streptogramins (J01F)	Quinolones (J01M)	Other antibacterials (J01X)	Sum (J01B, J01G, and J01R)*	Total (ATC group J01)
Belgium	0.01	0.73	0.37	0.04	0.11	0.17	0.12	0.02	1.57
Bulgaria	0.01	0.11	0.90	0.01	0.13	0.16	0.18	0.11	1.61
Croatia	0.03	0.47	0.53	0.04	0.16	0.24	0.24	0.09	1.80
Denmark	0.05	1.08	0.25	0.12	0.14	0.13	0.14	0.04	1.95
Estonia	0.04	0.55	0.51	0.05	0.17	0.11	0.11	0.02	1.56
Finland (a)	0.16	0.55	0.99	0.08	0.13	0.20	0.16	0.01	2.28
France	0.03	0.83	0.33	0.05	0.11	0.23	0.13	0.05	1.76
Greece	0.06	0.29	0.54	0.02	0.14	0.21	0.32	0.08	1.66
Hungary	0.03	0.27	0.37	0.03	0.12	0.19	0.08	0.02	1.12
Ireland	0.05	0.86	0.20	0.07	0.24	0.10	0.19	0.08	1.79
Italy	0.03	0.55	0.45	0.12	0.18	0.36	0.17	0.04	1.90
Latvia	0.13	0.42	0.60	0.07	0.13	0.26	0.22	0.05	1.88
Lithuania	0.05	0.71	0.77	0.00	0.08	0.18	0.27	0.05	2.12
Luxembourg	0.01	0.51	0.41	0.04	0.27	0.16	0.11	0.03	1.55
Malta	0.12	0.87	0.31	0.05	0.25	0.34	0.31	0.07	2.32
Netherlands	0.02	0.32	0.23	0.03	0.06	0.08	0.07	0.04	0.84
Norway	0.07	0.62	0.26	0.07	0.06	0.04	0.09	0.08	1.30
Poland	0.06	0.31	0.44	0.07	0.09	0.18	0.17	0.05	1.36
Portugal (b)	0.02	0.49	0.39	0.07	0.16	0.11	0.10	0.06	1.40
Slovakia	0.04	0.31	0.50	0.02	0.14	0.27	0.43	0.11	1.81
Slovenia	0.02	0.64	0.31	0.05	0.13	0.19	0.11	0.05	1.50
Spain	0.01	0.62	0.40	0.04	0.14	0.27	0.17	0.07	1.73
Sweden	0.16	0.99	0.17	0.04	0.06	0.14	0.08	0.02	1.65
United Kingdom	0.27	1.14	0.16	0.14	0.31	0.13	0.22	0.10	2.47
EU/EEA	0.08	0.67	0.37	0.07	0.16	0.21	0.17	0.06	1.79

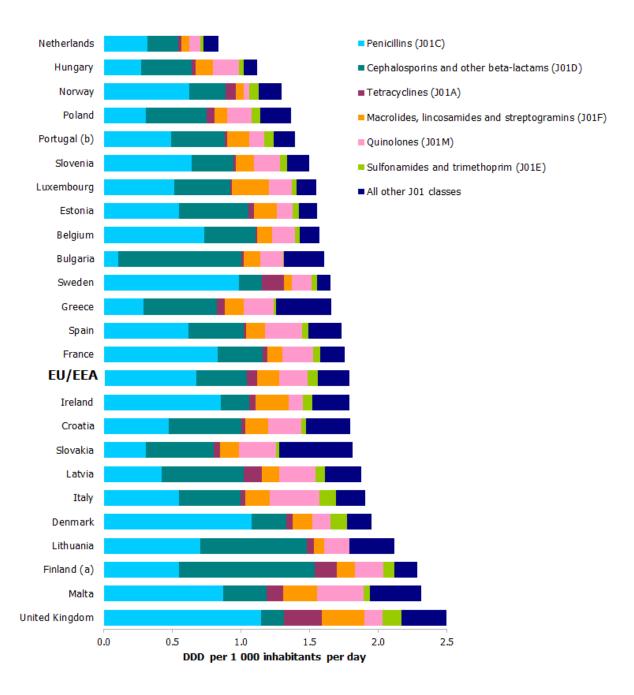
<sup>(</sup>a) Finland: data include consumption in remote primary healthcare centres and nursing homes.

EU/EEA refers to the corresponding population-weighted mean consumption based on countries that provided data for 2018.

<sup>(</sup>b) Portugal: data refer to public hospitals. Population was adjusted, based on hospital catchment area information provided by the country.

<sup>\*</sup>J01B: Amphenicols; J01G: Aminoglycoside antibacterials; J01R: Combinations of antibacterials

Figure 4. Consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, by country and ATC group in EU/EEA countries in 2018 (expressed as DDD per 1 000 inhabitants per day)



<sup>(</sup>a) Finland: data include consumption in remote primary healthcare centres and nursing homes.

EU/EEA refers to the corresponding population-weighted mean consumption based on countries that provided data for 2018.

The EU/EEA population-weighted mean consumption of antibacterials for systemic use in the hospital sector expressed as DDD per 1 000 inhabitants per day did not show any statistically significant trend during the period 2009–2018 (Table 6). Statistically significant increasing trends were observed for Bulgaria, Croatia, Denmark, Ireland Malta, Portugal and Sweden. A statistically significant decreasing trend was observed for Belgium, Finland, Latvia, Luxembourg and Norway.

<sup>(</sup>b) Portugal: data refer to public hospitals. Population was adjusted, based on hospital catchment area information provided by the country.

Table 6. Trends in consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, by country in EU/EEA countries, 2009–2018 (expressed as DDD per 1 000 inhabitants per day)

Country	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Trends in antimicrobial consumption, 2009–2018	CAGR Compound annual growth rate (%)	Trend
Netherlands		0.93	0.85	0.85	0.84	0.85	0.87	0.85	0.83	0.84	harran	-1.4%	
Hungary	1.15	1.21	1.08	1.11	1.08	1.13	1.11	1.07	1.13	1.12	1	-0.3%	
Norway	1.41	1.40	1.43	1.40	1.35	1.36	1.36	1.34	1.38	1.30	-	-1.0%	1
Poland						1.32	1.31	1.25	1.62	1.36		0.9%	
Portugal (b)	1.31	1.31	1.35	1.35	1.51	1.43	1.45	1.46	1.44	1.40		0.7%	1
Slovenia	1.60	1.54	1.48	1.39	1.38	1.43	1.49	1.45	1.47	1.50	-	-0.7%	
Luxembourg	1.94	1.90	1.84	1.83	1.82	1.64	1.61	1.57	1.62	1.55		-2.5%	1
Estonia	1.44	1.63	1.64	1.88	1.69	1.71	1.62	1.58	1.65	1.56	-	0.9%	
Belgium	1.77	1.76	1.76	1.70	1.64	1.62	1.64	1.64	1.62	1.57	-	-1.3%	1
Bulgaria	1.42	1.33	1.37	1.33	1.34	1.35	1.32	1.58	1.52	1.61	~~~~	1.3%	1
Sweden	1.41	1.45	1.53	1.57	1.60	1.49	1.59	1.56	1.51	1.65	- V	1.8%	1
Greece	3.02		1.78	1.66	1.79	1.87	1.91	2.15	2.07	1.66		-1.0%	
Spain								1.83	1.75	1.73	~	N/A	
France	1.81	1.82	1.74	1.73	1.76	1.79	1.77	1.76	1.73	1.76	~~~	-0.3%	
Ireland	1.24	1.60	1.61	1.58	1.59	1.48	1.71	1.66	1.60	1.79	7	4.2%	1
EU/EEA	1.77	1.78	1.74	1.75	1.71	1.75	1.78	1.81	1.77	1.79	~~~	0.2%	
Croatia	1.29	1.59	1.69	1.75	1.58	1.65	1.70	1.65	1.74	1.80	June 1	3.7%	1
Slovakia	1.70			1.85	2.03	2.30	2.22	2.31	1.45	1.81		-0.4%	
Latvia	2.16	2.65	2.08	1.98	1.96	1.94	1.94	1.83	1.89	1.88	^	-1.6%	1
Italy		1.87	2.00	2.13	1.87	1.86	2.09	2.21	1.89	1.90		0.3%	
Denmark	1.70	1.63	1.61	1.65	1.88	1.97	2.19	1.84	1.91	1.95		1.6%	1
Lithuania				2.06	1.98	1.96	2.15	2.12	2.12	2.12	~~~	0.5%	
Finland (a)	3.04	2.71	2.96	2.65	2.63	2.51	2.36	2.38	2.11	2.28	Your .	-3.1%	Ţ
Malta	1.24	1.80	1.53	1.31	1.56	1.95	2.49	2.52	2.78	2.32	and the same	7.2%	1
United Kingdom					2.07	2.23	2.19	2.21	2.24	2.47	and of	3.6%	1
Romania	2.46										•	N/A	

All country data are shown as they are reported to the European Surveillance System.

[light shaded cells] = linear regression was not applied for the highlighted cells and years with missing data.

EU/EEA refers to the corresponding population-weighted mean consumption based on reported antimicrobial consumption data of all 30 EU/EEA countries. Through imputation and other adjustments, the EU/EEA averages include the same number of EU/EEA countries for all years of the trend analyses (see the method chapter).

## Consumption of specific antimicrobial groups used for the treatment of patients infected with healthcare-associated resistant bacteria in the hospital sector

The EU/EEA population-weighted mean consumption of piperacillin-tazobactam (ATC J01CR05) showed a statistically significant increasing trend for the period 2009–2018, as was the case in two-thirds of the countries reporting hospital sector data.

In 2018, consumption of carbapenems (ATC group J01DH) was 0.04 DDD per 1 000 inhabitants per day (Table D11). Between 2009 and 2018, the EU/EEA population-weighted mean consumption of carbapenems did not show a statistically significant change (Table D10). A statistically significant increase was observed for six countries (Bulgaria, Croatia, Estonia, Hungary, Latvia and Malta). During the period 2009–2018, only Norway and Portugal showed a statistically significant decreasing trend.

The EU/EEA population-weighted mean consumption of polymyxins (ATC group J01XB) showed a statistically significant increase during 2009 and 2018 (Table D11). A statistically significant increase was observed for nine countries (Bulgaria, Denmark, Estonia, Hungary, Latvia, Norway, Portugal, Slovenia, Sweden). During 2009–2018, only Ireland showed a statistically significant decreasing trend. The EU/EEA population-weighted mean consumption of antimicrobials for the treatment of infections caused by multidrug-resistant gram-positive bacteria such as linezolid, daptomycin and tigecycline showed a statistically significant increasing trend for the period 2009-2018.

<sup>(</sup>a) Finland: data include consumption in remote primary healthcare centres and nursing homes.

All country data are shown as they are reported to the European Surveillance System.

<sup>(</sup>b) Portugal: data refer to public hospitals. Population was adjusted, based on hospital catchment area information provided by the country.

A statistically significant decrease in consumption of these antimicrobials was observed for more than half of the countries that continuously reported antimicrobials consumption data from the hospital sector between 2009 and 2018.

New antibacterial agents (e.g. combinations of cephalosporins and beta-lactamase inhibitors) have recently been authorised for use in the EU. Consumption of such antibacterial agents (ceftazidime-avibactam, ATC J01DD52 and ceftolozane-tazobactam, ATC J01DI54), was very low in 2018 but with an increasing number of countries reporting consumption; 19 and 24 EU/EEA countries respectively, in 2018 compared with 18 and 13 countries respectively in 2017.

### ECDC/EFSA/EMA secondary indicator for consumption of antibacterials for systemic use (ATC group J01) in the hospital sector

The proportion of glycopeptides, 3rd- and 4th-generation cephalosporins, monobactams, carbapenems, fluoroquinolones, polymyxins, piperacillin and enzyme inhibitor, linezolid, tedizolid and daptomycin out of the total hospital consumption of antibacterials for systemic use is presented in Table 7.

The average proportion was 32.5% and ranged from 17% in the United Kingdom to 58% in Bulgaria. During the period 2009–2018, statistically significant increasing trends were observed for the EU/EEA overall and seven countries specifically, whereas no country showed a statistically significant decreasing trend.

Table 7. The proportion of glycopeptides, 3rd- and 4th-generation cephalosporins, monobactams, carbapenems, fluoroquinolones, polymyxins, piperacillin and enzyme inhibitor, linezolid, tedizolid and daptomycin (DDD per 1 000 inhabitants per day) out of total hospital consumption of antibacterials for systemic use in EU/EEA countries, 2009–2018

Country	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Trends, 2009–2018	CAGR Compound annual growth rate (%)	Trend
Belgium	30.0	28.9	30.2	31.1	31.3	31.5	31.7	31.0	30.9	29.9	~	0.0%	
Bulgaria	37.7	45.2	51.0	55.2	52.7	57.5	55.2	59.8	58.1	57.5	-	4.8%	1
Croatia	34.5	29.9	26.2	26.5	27.8	31.0	31.7	30.9	32.2	32.2	-	-0.8%	
Denmark	19.2	20.1	20.7	21.3	22.7	22.6	20.6	23.7	21.4	22.9		2.0%	
Estonia	22.7	17.9	20.0	23.2	19.3	20.0	20.0	20.6	23.2	19.8	\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	-1.5%	
Finland (a)	20.9	19.3	18.9	19.0	22.2	22.7	21.9	22.9	23.2	19.4		-0.8%	
France	31.7	32.2	30.0	32.0	31.3	32.3	32.2	31.3	31.6	32.9	~~~	0.4%	
Greece	23.7		38.2	39.5	35.9	35.7	38.6	35.8	36.8	49.1	·	3.7%	
Hungary	34.8	36.1	37.4	37.2	37.8	37.4	38.8	39.4	40.1	40.6		1.7%	1
Ireland	25.9	25.8	25.9	26.3	32.3	36.9	29.5	30.1	29.4	28.7		1.1%	
Italy		47.2	42.7	44.2	49.1	48.4	42.8	37.0	48.6	48.4	~~~~~	0.3%	
Latvia	27.3	37.8	33.3	37.2	40.3	40.0	38.9	40.5	38.4	38.7	1	4.0%	1
Lithuania				26.8	19.6	20.4	25.2	24.9	24.6	22.5	\	-2.8%	
Luxembourg	29.5	30.0	29.7	31.3	31.1	31.8	33.3	36.0	34.0	32.2		1.0%	1
Malta	26.3	23.3	27.2	29.3	30.2	34.8	33.4	27.5	27.4	37.9		4.2%	
Netherlands		23.1	24.2	24.8	25.2	25.2	25.1	25.2	24.6	25.1	1	1.0%	
Norway	20.2	20.8	21.1	21.5	21.8	22.1	22.1	22.3	19.8	20.7		0.3%	
Poland						23.5	24.1	34.2	24.3	31.8	$\sim$	7.8%	
Portugal (b)	38.3	39.9	40.0	41.0	42.6	43.8	43.6	43.5	42.2	42.8		1.2%	1
Romania	29.5										•	N/A	
Slovakia	26.1			27.1	27.4	28.0	30.5	30.8	35.1	32.6		3.1%	1
Slovenia	31.7	32.0	33.2	32.4	31.5	32.1	32.8	33.1	32.2	31.4		-0.1%	
Spain								47.8	45.3	44.6	1	N/A	
Sweden	23.9	25.0	24.7	25.0	25.2	27.1	26.5	27.4	26.9	24.6	and the same	0.3%	
United Kingdom					15.8	16.7	17.4	17.6	16.6	16.7		1.1%	1
EU/EEA	29.1	29.6	29.2	30.3	30.9	31.3	30.5	30.5	31.2	32.5	-	1.2%	1

All country data are shown as they are reported to the European Surveillance System.

EU/EEA refers to the corresponding population-weighted mean consumption based on reported antimicrobial consumption data of all 30 EU/EEA countries. Through imputation and other adjustments, the EU/EEA averages include the same number of EU/EEA countries for all years of the trend analyses (see the method chapter).

<sup>(</sup>a) Finland: data include consumption in remote primary healthcare centres and nursing homes.

<sup>(</sup>b) Portugal: data refer to public hospitals. Population was adjusted, based on hospital catchment area information provided by the country.

<sup>[</sup>light shaded cells] = linear regression was not applied for the highlighted cells and years with missing data.

### Consumption of antibacterials from other ATC groups (A07A, P01A, J04A)

In 2018, hospital consumption of oral vancomycin (ATC A07AA09) and fidaxomicin (ATC A07AA12) was reported from 14 countries and ranged from  $2 \times 10^{-5}$  DDD per 1 000 inhabitants per day in Ireland to a maximum of 0.01 DDD per 1 000 inhabitants per day in Denmark.

Oral and rectal metronidazole (ATC P01AB01) consumption in hospitals was reported by 21 countries, ranging from 0.001 DDD per 1 000 inhabitants per day in Bulgaria to 0.05 DDD per 1 000 inhabitants per day in the United Kingdom.

Rifampicin (ATC J04AB02) consumption in 2018, reported in 19 countries, ranged from a minimum of 0.006 DDD per 1 000 inhabitants per day in Poland to a maximum of 0.13 DDD per 1 000 inhabitants per day in Latvia.

Consumption of oral vancomycin (A07AA09), rifampicin (J04AB02), and oral and rectal metronidazole (P01AB01) are presented in Table D13.

### Consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01B) in the community

In 2018, 26 countries reported data on consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01B) in the community (Table D14 and Figure D5).

The EU/EEA population-weighted mean consumption was 1.0 DDD per 1 000 inhabitants per day and consumption varied by a factor of 8, ranging from 0.38 (Croatia) to 3.0 DDD per 1 000 inhabitants per day (Belgium).

In 2018, terbinafine (D01B02), fluconazole (J02AC01), and itraconazole (J02AC02) comprised between 88% and 100% of the total consumption of antimycotics and antifungals for systemic use in the community among the reporting countries.

### Consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01B) in the hospital sector

In 2018, 21 countries reported data on consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01B) in the hospital sector (Table D15, Figure D8).

The EU/EEA population-weighted mean consumption was 0.16 DDD per 1 000 inhabitants per day. Consumption varied by a factor of seven, from 0.03 (Bulgaria) to 0.21 DDD per 1 000 inhabitants per day (France).

In 2018, fluconazole (J02AC01) accounted for 43% of the total consumption of antimycotics and antifungals for systemic use in the hospital sector among the reporting countries. Fluconazole consumption as a proportion of the total varied from 29% (Ireland) to 94% (Bulgaria).

### Consumption of antivirals for systemic use (ATC group J05) in both sectors (community and hospital sector)

Twenty-six countries reported data on antivirals for systemic use (ATC group J05) in 2018. The data are pooled for the two sectors (Table D16 and D17). Austria, Germany, Iceland and the Netherlands only reported data for the community.

The total EU/EEA population-weighted mean consumption of antivirals for systemic use (ATC group J05) for countries reporting data for both sectors was 2.47 DDD per 1 000 inhabitants per day and did not show any statistically significant trend during a five-year period 2014–2018 (Table D17

). Statistically significant increasing trends were observed for ten countries (Austria, Belgium, Bulgaria, Croatia, Denmark, Estonia, Finland, Latvia, Luxembourg and Sweden). No country showed a significantly decreasing trend.

Country-specific consumption showed a 13-fold difference from 0.51 DDD per  $1\ 000$  inhabitants per day in Malta to 6.78 in Estonia.

The EU/EEA population-weighted mean consumption in the reporting countries was the highest for combinations of antivirals to treat HIV infections (ATC group J05AR) (0.86 DDD per 1 000 inhabitants per day).

Table D17 and Figure D7 show the distribution of total consumption of antivirals for systemic use (ATC group J05) by their main indication: 'HIV/AIDS antivirals' 'HIV/hepatitis B antivirals', 'hepatitis B antivirals', 'hepatitis C antivirals', 'influenza antivirals' and one group for remaining substances. The EU/EEA population-weighted mean consumption of HIV/AIDS antivirals accounted for 55% of the total consumption of antivirals for systemic use (ATC group J05) in the reporting countries. The relative consumption of HIV/AIDS antivirals out of the total antiviral consumption ranged from 1.9% in Poland to 87% in Estonia.

Malta reported the highest proportion of HIV/hepatitis B antivirals consumed (44%), and Greece reported the highest proportion of hepatitis B antivirals consumed (25%).

The proportion of hepatitis C antivirals (new ATC group J05AP) consumed out of the total consumption of antivirals for systemic use (ATC group J05) ranged from 0.0% (Malta) to 15% (Italy). In 2018, direct-acting antivirals (DAA) were under surveillance within this group and 24 countries reported consumption of at least one DAA.

For herpes antivirals, the proportion of total consumption of antivirals for systemic use (ATC group J05) ranged from 0.02% (Italy) to 48% (Slovenia).

In 2018, the EU/EEA population-weighted mean consumption of substances used to treat influenza (rimantadine, J05AC02; zanamivir, J05AH01; oseltamivir, J05AH02) was 0.04 DDD per 1 000 inhabitants per day. The consumption ranged from <0.01 DDD per 1 000 inhabitants per day in Belgium, Hungary, Italy, Luxembourg;, Portugal and Slovakia to 0.46 DDD per 1 000 inhabitants per day in Lithuania, accounting for 45% of the total Lithuanian consumption of antivirals for systemic use.

#### **Discussion**

Reducing unnecessary and inappropriate use of antimicrobials is a public health priority. Controlling increasing antimicrobial resistance, both in the community and in the hospital sectoris the main aim of antimicrobial stewardship programmes (ASPs) worldwide. Measuring antimicrobial consumption is central to evaluating ASP effectiveness and identifying targets for interventions and is an essential element of any ASP. Effective ASPs should have developed tools to measure both the quantity and quality of antimicrobial use.

The ATC/DDD methodology has been used in this report as a standardised measurement for monitoring antimicrobial consumption [4,5,6]. Each year, EU/EEA countries report antimicrobial consumption data to ESAC-Net and these data are instrumental for the evaluation of ASPs and interventions at national and international level.

In June 2017, the European Commission adopted a new European One Health Action Plan against antimicrobial resistance [11]. The aim of this action plan is to support the EU and its Member States in delivering innovative, effective and sustainable responses to antimicrobial resistance. One of the key objectives of the action plan is to promote the prudent use of antimicrobials, which includes methods for data gathering and reporting on the sales and use of antimicrobials. The Action Plan notes that success should be measured through a limited number of key outcome indicators, based on data already collected.

To support EU Member States in their efforts to address antimicrobial resistance, the European Commission requested ECDC, EFSA and EMA to establish a list of harmonised outcome indicators for antimicrobial consumption and antimicrobial resistance. The chosen indicators had to take into account the 'One Health' approach and be suitable for evaluating progress made in reducing bacterial resistance to key antimicrobials in humans and animals. They also had to allow for evaluating improvements in the appropriateness and need for the use of antimicrobials in the EU. The indicators should be reconsidered at least every five years to determine whether they still reflect available data [7].

The primary antimicrobial consumption indicator, i.e. total consumption expressed as 'DDD per 1 000 inhabitants per day', as well as the two secondary outcome indicators have been used in this as in previous ESAC-Net reports. Results presented in this report should be interpreted with caution and used at the national level rather than for international benchmarking purposes. They may serve to evaluate antimicrobial stewardship interventions on the national level, but may also reflect the burden of infections caused by multidrug-resistant microorganisms.

The quality of antimicrobial consumption data depends on the type of data available for a given sector. For ESAC-Net, countries provide sales and/or reimbursement data and each data source has its advantages and limitations. The major limitation of reimbursement data is that antimicrobials dispensed without a prescription and non-reimbursed prescribed antimicrobials are not included [12]. For this reason, countries that report reimbursement data and are known to have a substantial proportion of antimicrobials dispensed without a prescription have been indicated in the tables and figures in this report. In addition, the type (source) of data in individual countries may change from one year to another, possibly affecting the results of patterns and trends in antimicrobial consumption.

In 2018, consumption of antibacterials for systemic use (ATC group J01) in the community within the EU/EEA varied between countries with a north-to-south gradient. There are many reasons for these large differences, some of which are cultural determinants.

The EU/EEA population-weighted mean consumption of antibacterials for systemic use (ATC group J01) in the community did not show any statistically significant change during the period 2009–2018. In contrast to previous years, only one country showed a statistically significant increasing ten-year trend and an increasing number of countries reported a statistically significant decreasing ten-year trend in the consumption of antibacterials for systemic use (i.e. nine countries in this report compared to four countries in the last report of 2016).

In addition, a statistically significant increasing trend of EU/EEA population-weighted mean consumption was only reported for ATC group J01X (this group includes glycopeptides) and statistically decreasing trends were observed for three subgroups tetracyclines (ATC J01A), macrolides, lincosamins and streptogramins (ATC J01F) and for quinolones (ATC J01M). For quinolones, 14 countries, i.e. more than half of the countries that continuously reported data between 2009 and 2018, reported a statistically significant decreasing trend in the community consumption of quinolones. These ten-year trends (2009–2018) in the consumption of antibacterials for systemic use in the community may reflect antimicrobial stewardship activities in EU/EEA countries, including awareness campaigns connected to the European Antibiotic Awareness Day after its introduction in 2008.

Since patients are not treated with antibiotics continuously every day of the year, a more understandable way of illustrating the meaning of the indicator DDD per 1 000 inhabitants per day may be the 'number of DDD per person (inhabitant) per year'. An estimate of the number of days annually for which, on average, each person is treated with an antibiotic can easily be calculated from the indicator DDD per 1 000 inhabitants per day by dividing the figure by 1 000 (population) and multiplying it by 365 (days in a year) or, shortened, by multiplying the figure by 0.365. In 2018 for the EU/EEA, there were about seven DDD per person per year for antibacterials for systemic use in the community. In other words, on average in 2018, each person in the EU/EAA was treated with an antibiotic for approximately seven days, which in most cases corresponds to one antibiotic course per year.

Any ranking of the countries based on the 'consensus-based quality indicators' should be interpreted with caution, as the indicators are not independent. For example, an increase in the consumption of macrolides, lincosamides and streptogramins will probably result in an increase in the ratio of broad-spectrum penicillins, cephalosporins and macrolides to narrow-spectrum penicillins, cephalosporins and erythromycin. For countries where changes in the ranking suggest quality improvement, this may reflect a relative change compared with other countries. For example, quality may have decreased in all countries but less so in the specific country in question [13]. It should be emphasised that these indicators cannot by themselves indicate quality of antimicrobial use in the community, unless they are combined with corresponding clinical data (e.g. indications, antimicrobial resistance patterns, current national programmes such as guidelines, restrictions).

The types of healthcare facilities included in the hospital sector differ across EU/EEA countries, thus caution should be exercised when interpreting the results, especially in comparison between countries. For example, hospital data from Finland include consumption from nursing homes and remote primary healthcare centres. In the United Kingdom, on average, patients have shorter lengths of hospital stay than in other EU/EEA countries and, when antimicrobials are prescribed, there is a policy of dispensing, via the hospital pharmacy, a full course of antimicrobials to patients discharged from the hospital. Consequently, in both countries hospital consumption rates are relatively higher and community consumption relatively lower.

In contrast to prescribing practices in the community, penicillins were not the most frequently prescribed antibacterial group in the hospital sector for all countries, and the proportions of cephalosporins, other betalactams (including carbapenems) and other groups of antimicrobials were generally higher than in the community. However, the appropriateness of antimicrobial consumption cannot be judged based on the consumption data only, and needs to be assessed at a national level taking into account national policies, guidelines and resistance levels.

Inappropriate antibacterial prescribing in hospitals promotes the emergence and spread of multidrug-resistant (MDR) bacteria responsible for healthcare-associated infections, and is a global healthcare issue [14,15]. The prevalence of antibiotic-resistant bacteria, including multidrug-resistant strains is increasing, especially in hospitals where selective antibiotic pressure is present. Infections caused by these bacteria have become a serious threat, as there are fewer or sometimes no effective antimicrobial agents available.

Penicillins combined with beta-lactamase inhibitors (e.g. piperacillin-tazobactam) represent a group of antibiotics available for the treatment of infections caused by extended-spectrum beta-lactamase (ESBL)-producing gramnegative bacteria. However, they are ineffective against carbapenem-resistant gram-negative bacteria.

Carbapenems are a last-line group of antimicrobials and are mainly used in hospitals to treat patients with confirmed or suspected serious infections involving multidrug-resistant gram-negative bacteria. Previous use of carbapenems is a risk factor for subsequent infection with carbapenem-resistant bacteria such as carbapenem-resistant *Enterobacteriaceae* (CRE), often through production of a carbapenemase enzyme, carbapenem-resistant *Acinetobacter baumannii* or carbapenem-resistant *Pseudomonas aeruginosa*. Carbapenem-resistant bacteria are highly drug-resistant and only a few antibiotic groups such as polymyxins (mainly colistin), are available for the treatment of patients infected with such bacteria [16,17].

The second Joint Interagency Antimicrobial Consumption and Resistance Analysis (JIACRA) report from ECDC, EFSA and EMA showed a strong association between carbapenem consumption and the percentage of carbapenem resistance in *Klebsiella pneumoniae* isolates from invasive infections in EU/EEA countries reporting these data [18].

The impact of global shortages of piperacillin-tazobactam in 2016 and 2017 on consumption of antibacterials for systemic use in EU/EEA countries is unknown, but it certainly represented a challenge to antimicrobial stewardship teams that had to provide guidance on alternative treatments.

This shortage could have caused a shift towards increased consumption of third- and fourth-generation cephalosporins and of carbapenems, but this was not the case with the EU/EEA population-weighted mean and would need to be assessed at national level in each country.

One third of the countries having reported data continuously between 2009 and 2018 reported a statistically significant increasing trend in carbapenem consumption, but these increases did not affect the trend of the EU/EEA population-weighted mean consumption over the past ten years. This finding is consistent with the 2018 data from the European Antimicrobial Resistance Surveillance Network (EARS-Net), which show that the population-weighted EU/EEA mean percentage of carbapenem resistance in *Klebsiella pneumoniae* invasive isolates has been stable in recent years [19].

The occurrence of statistically significant increasing ten-year-trends of the EU/EEA population-weighted mean consumption of certain antimicrobials (e.g. linezolid, daptomycin and tigecycline for the treatment of infections caused by multidrug-resistant gram-positive bacteria), is consistent with data from EARS-Net. This data showed increasing EU/EEA population-weighted mean percentages of vancomycin resistance in *Enterococcus faecium* invasive isolates (from 10.5% in 2015 to 17.3% in 2018), as well as corresponding increasing trends in almost half of the countries.

Assuming that the average duration of one carbapenem treatment is ten days, the consumption of 0.04 DDD per 1 000 inhabitants per day corresponds to around 800 000 carbapenem treatment courses administered in the EU/EEA each year.

The EU/EEA population-weighted mean trend in consumption of fluoroquinolones is decreasing, although some countries still show an increasing trend in the consumption of this group. On 11 March 2019, the European Commission issued a legally binding decision regarding the use of fluoroquinolones based on EMA's recommendation, i.e. the marketing authorisation of medicines containing cinoxacin, flumequine, nalidixic acid, and pipemidic acid is suspended, and the use of the remaining fluoroquinolones should be restricted because of risk of disabling and potentially permanent side-effects. According to EMA's recommendation, fluoroquinolones should not be used (a) to treat infections that might get better without treatment or infections which are not severe (such as throat infections); (b) to treat non-bacterial infections, e.g. non-bacterial (chronic) prostatitis; (c) for preventing traveller's diarrhoea or recurring lower urinary tract infections (urine infections that do not extend beyond the bladder); (d) to treat mild or moderate bacterial infections unless other antibacterial medicines commonly recommended for these infections cannot be used. National authorities will enforce this decision for the fluoroquinolone and quinolone medicines authorised in their countries and they will also take other appropriate measures to promote the correct use of these antibiotics \(^1\).

As expected, the consumption pattern of antimycotics and antifungals for systemic use in the hospital sector differed from that in the community due to different aetiology and variations in the diseases and disease severity treated in the sectors. In the hospital sector, the antimycotic with the highest consumption was fluconazole, as opposed to terbinafine in the community.

Within the ATC groups of antimicrobials for systemic use (ATC groups J01, J02 & D01B, and J05), antivirals for systemic use (ATC group J05) showed the highest variation among countries. A five-year trend analysis, provided for the first time in this report, did not show a significant trend at EU/EEA level, but statistically increasing trends were reported by ten countries. An increasing number of countries are reporting consumption of direct acting antivirals for the treatment of HCV infection. As shown with antibacterials for systemic use (ATC group J01), future data analyses may highlight certain socioeconomic or structural determinants that would explain such variation. Countries are encouraged to report data on antiviral consumption for systemic use to TESSy.

Finally, in 2019, the DDDs for nine antimicrobials and routes of administration were set to higher values by the WHO Collaborating Centre for Drug Statistics Methodology. As a result, consumption of respective antimicrobial groups as well as total antimicrobial consumption may appear to be lower than in previous ECDC reports on antimicrobial consumption. The largest impact of this change was seen for penicillins and ranking of countries in the EU/EEA benchmark. To avoid misinterpretation of antimicrobial consumption, readers should always consult the latest annual epidemiological report where ten-years trends in antimicrobial consumption are displayed taking into account the latest DDD update.

<sup>&</sup>lt;sup>1</sup> https://www.ema.europa.eu/en/medicines/human/referrals/quinolone-fluoroquinolone-containing-medicinal-products

#### **Public health conclusions**

Antimicrobial resistance is an increasing threat to public health leading to an estimated 33 000 deaths attributable to infections with antibiotic-resistant bacteria each year in the EU/EEA, and antimicrobial consumption is a primary driver of resistance. Antimicrobial stewardship programmes aim to improve antimicrobial use in order to prevent emergence of antimicrobial resistance and improve patient outcomes. The main aims of ASPs are continuous monitoring of antimicrobial resistance and antimicrobial consumption. As antimicrobial resistance patterns and trends differ across countries, so do the extent, pattern and trends of antimicrobial consumption. Thus, understanding antimicrobial resistance epidemiology in the EU/EEA requires reliable antimicrobial consumption data from each EU/EEA country.

Excessive antibiotic use in hospitals promotes the emergence and spread of multidrug-resistant bacteria responsible for healthcare-associated infections. Use of broad-spectrum antimicrobials creates the greatest selective pressure for the development of multi-drug resistance, in particular in gram-negative bacteria. In the community, the decreasing trends for consumption of a frequently used antimicrobial group may be the result of national initiatives, e.g. awareness campaigns, promoting prudent use of antimicrobials, during the past years. In the hospital sector, although there was no statistically significant trend at the EU level in the consumption of all last-line groups of antimicrobials such as carbapenems, several EU/EEA countries showed a statistically significant increasing trend in the consumption of these antimicrobials. This observation suggests that the current efforts to implement ASPs may need to be intensified in some countries.

To combat increasing antimicrobial resistance within a 'One-Health' approach, EU/EEA countries agreed to develop their own national action plans, including ASP strategies based on national surveillance of antimicrobial consumption and antimicrobial resistance [20].

#### References

- 1. European Centre for Disease Prevention and Control. Introduction to the Annual epidemiological report. Stockholm: ECDC; 2019. Available from: <a href="https://ecdc.europa.eu/en/annual-epidemiological-reports/methods">https://ecdc.europa.eu/en/annual-epidemiological-reports/methods</a>
- European Centre for Disease Prevention and Control. Surveillance systems overview for 2017 [internet, downloadable spreadsheet]. Stockholm: ECDC; 2019. Available from: <a href="https://ecdc.europa.eu/en/publications-data/surveillance-systems-overview-2017">https://ecdc.europa.eu/en/publications-data/surveillance-systems-overview-2017</a>
- European Centre for Disease Prevention and Control. Antimicrobial consumption database (ESAC-Net)
  [internet]. Stockholm: ECDC; 2019. Available from: <a href="https://ecdc.europa.eu/en/antimicrobial-consumption/surveillance-and-disease-data/database">https://ecdc.europa.eu/en/antimicrobial-consumption/surveillance-and-disease-data/database</a>
- 4. WHO Collaborating Centre for Drug Statistics Methodology. ATC Index with DDDs. Oslo, WHO 2019 Available from: https://www.whocc.no/atc\_ddd\_index/
- 5. Versporten A, Gyssens IC, Pulcini C, Monnier AA, Schouten J, Milanič R, et al. Metrics to assess the quantity of antibiotic use in the outpatient setting: a systematic review followed by an international multidisciplinary consensus procedure. Journal of Antimicrobial Chemotherapy. 2018 Jun 1;73(suppl\_6):vi59-66.
- 6. Stanić Benić M, Milanič R, Monnier AA, Gyssens IC, Adriaenssens N, Versporten A, et al, the DRIVE-AB WP1 group; Metrics for quantifying antibiotic use in the hospital setting: results from a systematic review and international multidisciplinary consensus procedure, Journal of Antimicrobial Chemotherapy, Volume 73, Issue suppl 6, 1 June 2018, Pages vi50–vi58.
- ECDC (European Centre for Disease Prevention and Control), EFSA BIOHAZ Panel (European Food Safety Authority Panel on Biological Hazards) and CVMP (EMA Committee for Medicinal Products for Veterinary Use), 2018. ECDC, EFSA and EMA Joint Scientific Opinion on a list of outcome indicators as regards surveillance of antimicrobial resistance and antimicrobial consumption in humans and food-producing animals. EFSA Journal 2018;15(10):5017, 70 pp. Available from: <a href="https://doi.org/10.2903/j.efsa.2018.5017">https://doi.org/10.2903/j.efsa.2018.5017</a>.
- 8. Coenen S, Ferech M, Haaijer-Ruskamp FM, Butler CC, Vander Stichele RH, Verheij TJ, et al. European Surveillance of Antimicrobial Consumption (ESAC): quality indicators for outpatient antibiotic use in Europe. Qual Saf Health Care. 2007 Dec;16(6):440-5
- 9. Van Boeckel TP, Gandra S, Ashok A, Caudron Q, Grenfell BT, Levin SA, Laxminarayan R. Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data. The Lancet Infectious Diseases. 2014 Aug 1;14(8):742-50.
- European Centre for Disease Prevention and Control. Antimicrobial consumption surveillance in Europe 2013-2014. Annual report of the European Antimicrobial Consumption Surveillance Network (ESAC-Net). Stockholm: ECDC; 2014. Available from <a href="https://www.ecdc.europa.eu/en/publications-data/surveillance-antimicrobial-consumption-europe-2013-2014">https://www.ecdc.europa.eu/en/publications-data/surveillance-antimicrobial-consumption-europe-2013-2014</a>
- 11. European Commission 2018. A European One Health Action Plan against Antimicrobial resistance (AMR) EC; 2018. Available from: <a href="https://ec.europa.eu/health/amr/sites/amr/files/amr action plan 2018 en.pdf">https://ec.europa.eu/health/amr/sites/amr/files/amr action plan 2018 en.pdf</a>
- 12. Safrany N, Monnet DL. Antibiotics obtained without a prescription in Europe. Lancet Infect Dis. 2012 Mar;12(3):182-3
- 13. Borg MA. Cultural determinants of infection control behaviour: understanding drivers and implementing effective change. J Hosp Infect. 2014 Mar:86(3):161-8.
- 14. Adriaenssens N, Coenen S, Versporten A, Muller A, Vankerckhoven V, Goossens H. European Surveillance of Antimicrobial Consumption (ESAC): quality appraisal of antibiotic use in Europe. J Antimicrob Chemother. 2011 Dec;66 Suppl 6:vi71-7
- 15. Magiorakos AP, Burns K, Rodriguez Bano J, Borg M, Daikos G, Dumpis U, et al. Infection prevention and control measures and tools for the prevention of entry of carbapenem-resistant *Enterobacteriaceae* into healthcare settings: guidance from the European Centre for Disease Prevention and Control. Antimicrobial resistance and infection control. 2018;6:113.
- European Centre for Disease Prevention and Control. Proposals for EU guidelines on the prudent use of antimicrobials in humans. Stockholm: ECDC; 2018 https://ec.europa.eu/health/amr/sites/amr/files/amr guidelines prudent use en.pdf

- 17. European Centre for Disease Prevention and Control. Carbapenem-resistant Enterobacteriaceae second update; 26 September 2019. Stockholm: ECDC; 2019. Available from: <a href="https://www.ecdc.europa.eu/sites/default/files/documents/carbapenem-resistant-enterobacteriaceae-risk-assessment-rev-2.pdf">https://www.ecdc.europa.eu/sites/default/files/documents/carbapenem-resistant-enterobacteriaceae-risk-assessment-rev-2.pdf</a>
- 18. ECDC (European Centre for Disease Prevention and Control), EFSA (European Food Safety Authority), and EMA (European Medicines Agency), 2018. ECDC/EFSA/EMA second joint report on the integrated analysis of the consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals Joint Interagency Antimicrobial Consumption and Resistance Analysis (JIACRA) Report. EFSA Journal 2018;15(7):4872, 135 pp. doi:10.2903/j.efsa. 2018.4872. Available from: <a href="https://ecdc.europa.eu/sites/portal/files/documents/efs2">https://ecdc.europa.eu/sites/portal/files/documents/efs2</a> 4872 final.pdf
- 19. European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2019. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Stockholm: ECDC; 2019. Available from: <a href="https://www.ecdc.europa.eu/en/publications-data/surveillance-antimicrobial-resistance-europe-2018">https://www.ecdc.europa.eu/en/publications-data/surveillance-antimicrobial-resistance-europe-2018</a>
- 20. The Council of the European Union: Council conclusions on the next steps towards making the EU a best practice region in combatting antimicrobial resistance. Official Journal of the European Union 2019/C 214/01; 25 June 2019. Available from:
  - https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=OJ:C:2019:214:FULL&from=E

### **Downloadable tables and figures**

#### **Tables**

**Table D1**. Trends in consumption of tetracyclines (ATC group J01A) in the community, EU/EEA countries, 2009–2018, expressed as DDD per 1 000 inhabitants per day

**Table D2**. Trends in consumption of beta-lactam antibacterials, penicillins (ATC group J01C) in the community, EU/EEA countries, 2009–2018, expressed as DDD per 1 000 inhabitants per day

**Table D3**. Trends in consumption of other beta-lactam antibacterials (ATC group J01D) in the community, EU/EEA countries, 2009–2018, expressed as DDD per 1 000 inhabitants per day

**Table D4.** Trends in consumption of sulfonamides and trimethoprim (ATC group J01E) in the community, EU/EEA countries, 2009–2018, expressed as DDD per 1 000 inhabitants per day

**Table D5**. Trends in consumption of macrolides, lincosamides and streptogramins (ATC group J01F) in the community, EU/EEA countries, 2009–2018, expressed as DDD per 1 000 inhabitants per day

**Table D6**. Trends in consumption of quinolone antibacterials (ATC group J01M) in the community, EU/EEA countries, 2009–2018, expressed as DDD per 1 000 inhabitants per day

**Table D7**. Trends in consumption of other antibacterials (ATC group J01X) in the community, EU/EEA countries, 2009–2018, expressed as DDD per 1 000 inhabitants per day

**Table D8.** ESAC quality indicators for consumption data of antibacterials for systemic use (ATC group J01), for the community, EU/EEA countries, 2018

**Table D9**. Consumption of oral vancomycin (A07AA09), rifampicin (J04AB02) and oral and rectal metronidazole (P01AB01) in the community, EU/EEA countries, 2018, expressed as DDD per 1 000 inhabitants per day

**Table D10**. Trends in consumption of carbapenems (ATC group J01DH) in the hospital sector, EU/EEA countries, 20013–2018, expressed as DDD per 1 000 inhabitants per day

**Table D11**. Trends in consumption of polymyxins (ATC group J01XB) in the hospital sector, EU/EEA countries, 2009–2018, expressed as DDD per 1 000 inhabitants per day

**Table D12.** Consumption of oral vancomycin (A07AA09), rifampicin (J04AB02) and oral and rectal metronidazole (P01AB01) in the hospital sector, EU/EEA countries, 2018, expressed as DDD per 1 000 inhabitants per day

**Table D13.** Consumption of antimycotics (ATC group J02) and antifungals (ATC group D01B) for systemic use in the community, EU/EEA countries, 2018, expressed as DDD per 1 000 inhabitants per day

**Table D14**. Consumption of antimycotics (ATC group J02) and antifungals (ATC group D01B) for systemic use in the hospital sector, EU/EEA countries, 2018, expressed as DDD per 1 000 inhabitants per day

**Table D15**. Consumption of antivirals for systemic use (ATC group J05) in both sectors (community and hospital sector), EU/EEA countries, 2018, expressed as DDD per 1 000 inhabitants per day

**Table D16**. Consumption of antivirals for systemic use (ATC group J05) in both sectors (community and hospital sector), **grouped into categories of their main indication**, EU/EEA countries, 2018, expressed as DDD per 1 000 inhabitants per day

**Table D17**. Trends in consumption of antivirals for systemic use (ATC group J05) in the community, EU/EEA countries, 2009–2018, expressed as DDD per 1 000 inhabitants per day

**Table D18.** Consumption of antibacterials for systemic use (ATC group J01) in the community, EU/EEA countries, 1997–2018, expressed as DDD per 1 000 inhabitants per day **and calculated with the ATC/DDD index 2019** 

**Table D19.** Consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, EU/EEA countries, 1997–2018, expressed as DDD per 1 000 inhabitants per day **and calculated with the ATC/DDD index 2019** 

#### **Figures**

**Figure D1**. Consumption of broad- and narrow-spectrum penicillins (ATC group J01C) for systemic use in the community, EU/EEA countries, 2018, expressed as DDD per 1 000 inhabitants per day

**Figure D2.** Consumption of first-, second-, third- and fourth-generation cephalosporins (ATC group J01DB-DE) for systemic use in the community, EU/EEA countries, 2018, expressed as DDD per 1 000 inhabitants per day

**Figure D3.** Consumption of short-, intermediate- and long-acting macrolides (ATC group J01F) for systemic use in the community, EU/EEA countries, 2018, expressed as DDD per 1 000 inhabitants per day

**Figure D4. C**onsumption of first-, second- and third-generation quinolones (ATC group J01M) for systemic use in the community, EU/EEA countries, 2018, expressed as DDD per 1 000 inhabitants per day

**Figure D5**. Consumption of antimycotics (ATC group J02) and antifungals (ATC group D01B) for systemic use in the community, EU/EEA countries, 2018, expressed as DDD per 1 000 inhabitants per day

**Figure D6**. Consumption of antimycotics (ATC group J02) and antifungals (ATC group D01B) for systemic use in the hospital sector, EU/EEA countries, 2018, expressed as DDD per 1 000 inhabitants per day

**Figure D7.** Consumption of antivirals for systemic use (ATC group J05) in both sectors (community and hospital sector), grouped into categories of their main indication, EU/EEA countries, 2018, expressed as DDD per 1 000 inhabitants per day

#### **Annex**

Annex 1. Further sub-classification of macrolides, quinolones and antivirals (2019 ATC/DDD index)