



## SURVEILLANCE REPORT

Annual Epidemiological Report for 2017

# Antimicrobial consumption

## Introduction

### Key facts

- Twenty-seven countries, comprising 25 EU Member States and two EEA countries (Iceland and Norway) reported data on antimicrobial consumption for 2017. Twenty-two countries reported both community and hospital consumption, three countries reported only community consumption, and two countries reported total consumption in both sectors 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) Index with DDDs 2018 was used for the analysis.
- In 2017, the average total consumption (community and hospital sector) of antibacterials for systemic use (ATC group J01) in the EU/EEA was 23.4 DDD per 1 000 inhabitants per day (country range: 11.0–34.1).
- In the community, the average consumption of antibacterials for systemic use was 21.8 DDD per 1 000 inhabitants per day (country range: 10.1–33.6). During the period 2013–2017, no statistically significant change was observed for the EU/EEA overall and no country reported a statistically significant increasing trend. However, statistically decreasing trends were observed for Finland, Germany, Italy, Luxembourg, the Netherlands, Norway, Sweden and the United Kingdom.
- 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 2.25 (country range: 0.1–22.2).
- The average consumption of antimycotics and antifungals for systemic use (ATC groups J02 and D01B) in the community was 0.9 DDD per 1 000 inhabitants per day (country range: 0.38–3.0).
- In the hospital sector, the average consumption of antibacterials for systemic use was 2.0 DDD per 1 000 inhabitants per day (country range: 0.9–3.1). During the period 2013–2017, no statistically significant change was observed for the EU/EEA overall. However, statistically significant increasing trends were observed for Croatia and Malta, and a statistically significant decreasing trend was observed for Finland.
- The average consumption of carbapenems in the hospital sector was 0.06 DDD per 1 000 inhabitants per day (country range: 0.02–0.17) and this did not change significantly between 2013 and 2017. However, statistically significant increasing trends were observed for nine countries and two countries reported a statistically significant decreasing trend.

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- The average consumption of polymyxins in the hospital sector was 0.024 DDD per 1 000 inhabitants per day (country range: <0.001–0.105). This did not change significantly between 2013 and 2017. Statistically significant increasing trends were observed for three countries and statistically significant decreasing trends in two countries.
- The average proportion of glycopeptides, 3rd- and 4th-generation cephalosporins, monobactams, carbapenems, fluoroquinolones, polymyxins, piperacillin and enzyme inhibitor, linezolid, tedizolid and daptomycin out of the total consumption of antibacterials for systemic use in the hospital sector was 30.4% (country range: 15.6–58.5%).
- The average consumption of antimycotics and antifungals for systemic use in the hospital sector (ATC groups J02 and D01B) was 0.08 DDD per 1 000 inhabitants per day (country range: 0.03–0.19).
- The average consumption of antivirals for systemic use (ATC group J05) in both sectors (community and hospital sector) was 2.0 DDD per 1 000 inhabitants per day (country range: 0.22–6.9).
- The most recent data on antimicrobial consumption are available from the public [ESAC-Net interactive database](#) (data for 1997–2017) on the ECDC website.

## Methods

This report is based on data for 2017 retrieved from The European Surveillance System (TESSy) on 23 October 2018 and a re-upload of data for ATC subgroups from Spain and Slovenia on 13 November 2018. TESSy is a system for the collection, analysis and dissemination of data on communicable diseases. For a detailed description of methods used to produce this report, please refer to the Methods chapter in the Introduction to the Annual epidemiological report [1].

An overview of the national surveillance systems is available online [2] and 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 for 2017 collected at European level. Twenty-five EU Member States and two EEA countries (Iceland and Norway) reported antimicrobial consumption data at the European level. For this report, the data sources for antimicrobial consumption were the same as in the previous report, with the exception of Spain which, in addition to reimbursement data, also reported sales data for 2016 and 2017 and, for the first time, data from the hospital sector [3].

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 2018 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 different strengths into units of measurement of active substances.

There are three major categories of antimicrobials under surveillance. These are 1) antibacterials for systemic use (ATC group J01), 2) antimycotics and antifungals for systemic use (ATC groups J02 & D01B) and 3) 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. Thus, vancomycin and fidaxomicin for oral administration are classified as intestinal anti-infectives in the group A07A, and are used against *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 the group P01A. Rifampicin is classified as a drug for the treatment of tuberculosis (J04A). In clinical practice, rifampicin is also used for *Haemophilus influenzae* infections or in combination with other antibacterials to treat methicillin-resistant *Staphylococcus aureus* (MRSA) infections, brucellosis, Legionnaires' disease and serious staphylococcal infections.

Consumption data were collected for the community (primary care) and hospital (secondary care and tertiary care) sectors as a detailed list of all available antimicrobial products (register) and the annual number of packages used, or, if unavailable, as the number of DDD per ATC substance and route of administration. Consumption of antibacterials for systemic use and 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 aggregated.

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) and in the hospital sector. It gives a rough estimate of the proportion of the population treated daily with antimicrobials. It has been recommended as a main indicator for monitoring outpatient antibiotic consumption by the EU-funded project 'Driving re-investment in R&D and responsible antibiotic use' (DRIVE AB) [5].

Although the ATC/DDD methodology [4] and the DRIVE AB project [6] recommend presenting hospital consumption as the number of DDDs per 100 bed-days, in this report the indicator DDD per 1 000 inhabitants per day was applied for both the community and the hospital sector because denominator data on the total number of occupied bed-days are currently not available for most EU/EEA countries. In addition, presenting data with the same denominator enables cross-sectoral comparison. This indicator has recently 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 hospital and community sector [7].

The pattern of antibacterial consumption was also presented through the secondary harmonised outcome indicators agreed 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 within the total hospital consumption of antibacterials for systemic use.

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

The ATC/DDD methodology and the DRIVE AB project do not recognise the number of packages as a relevant and valid indicator for monitoring the pattern and trends in antibacterial consumption. However, where countries provided the number of packages of antibacterials for oral use consumed in the community as part of the metadata, the indicator - 'packages per 1 000 inhabitants per day' was applied. This indicator may serve as a proxy for the number of prescriptions only at the national level, provided that one antibiotic package is prescribed per prescription encounter.

Consumption displayed with the label 'EU/EEA' is based on the mean of the data from all ESAC-Net participating countries reported for a particular 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. The five-year trends for consumption expressed as DDD per 1 000 inhabitants per day were assessed using linear regression.

More details on the methods, collection, validation and reporting of European antimicrobial consumption data are available from the [ESAC-Net pages](#) on ECDC's website. They are also described in the [ESAC-Net surveillance reports](#) [9]. The most recent data on antimicrobial consumption are available from the public [ESAC-Net interactive database](#) (data for 1997–2017) on ECDC's website [3].

Finally, the ATC Index with DDDs 2019 [10] will include substantial alterations in DDDs for eight antibacterials (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, 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). Therefore, the new DDDs will be applied to all historic and future antibiotic consumption data from January 2019 onwards. The impact of changes in DDDs on the pattern of antibiotic consumption for 2017 consumption data is also presented in this report.

## Antimicrobial consumption

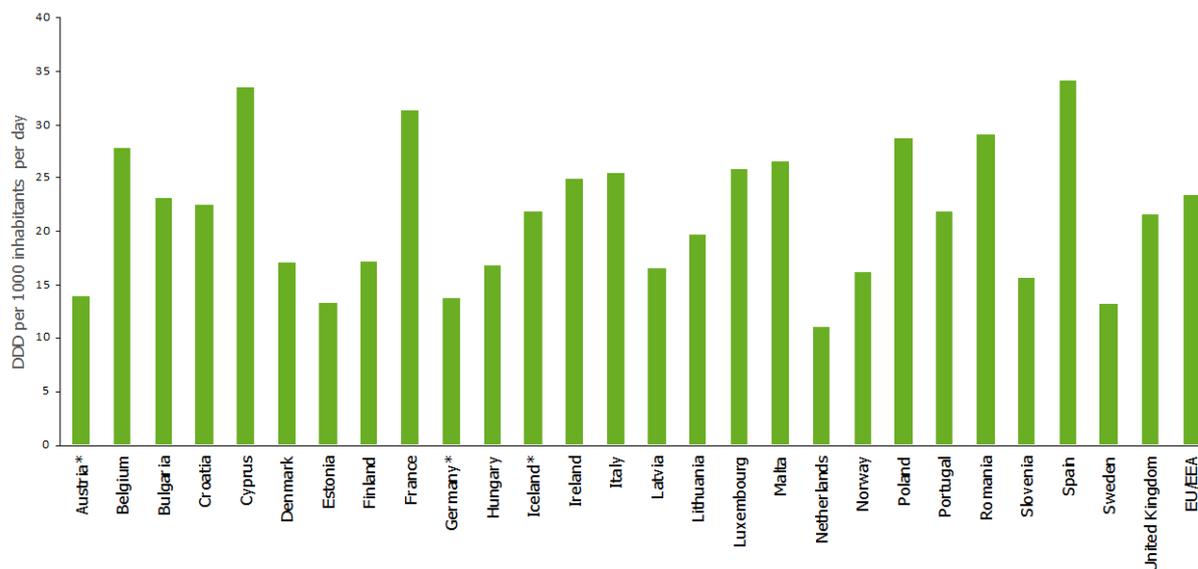
All EU Member States (except the Czech Republic, Greece and Slovakia) and two EEA countries (Iceland and Norway) reported antimicrobial consumption in 2017. Twenty-two countries reported both community and hospital consumption, three countries (Austria, Germany and Iceland) reported only community consumption, and two countries (Cyprus and Romania) reported total consumption in both sectors without differentiating between them. Nevertheless, data from these two countries are shown together with community consumption from other countries because, on average, approximately 90% of the total antibacterial consumption data 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 J01) in humans

In 2017, the EU/EEA population-weighted mean total consumption (community and hospital sector) of antibacterials for systemic use was 23.4 DDD per 1 000 inhabitants per day, ranging from 11.0 in the Netherlands to 34.1 in Spain (Figure 1).

**Figure 1. Total consumption of antibacterials for systemic use (ATC group J01), EU/EEA countries, 2017, expressed as DDD per 1 000 inhabitants per day**



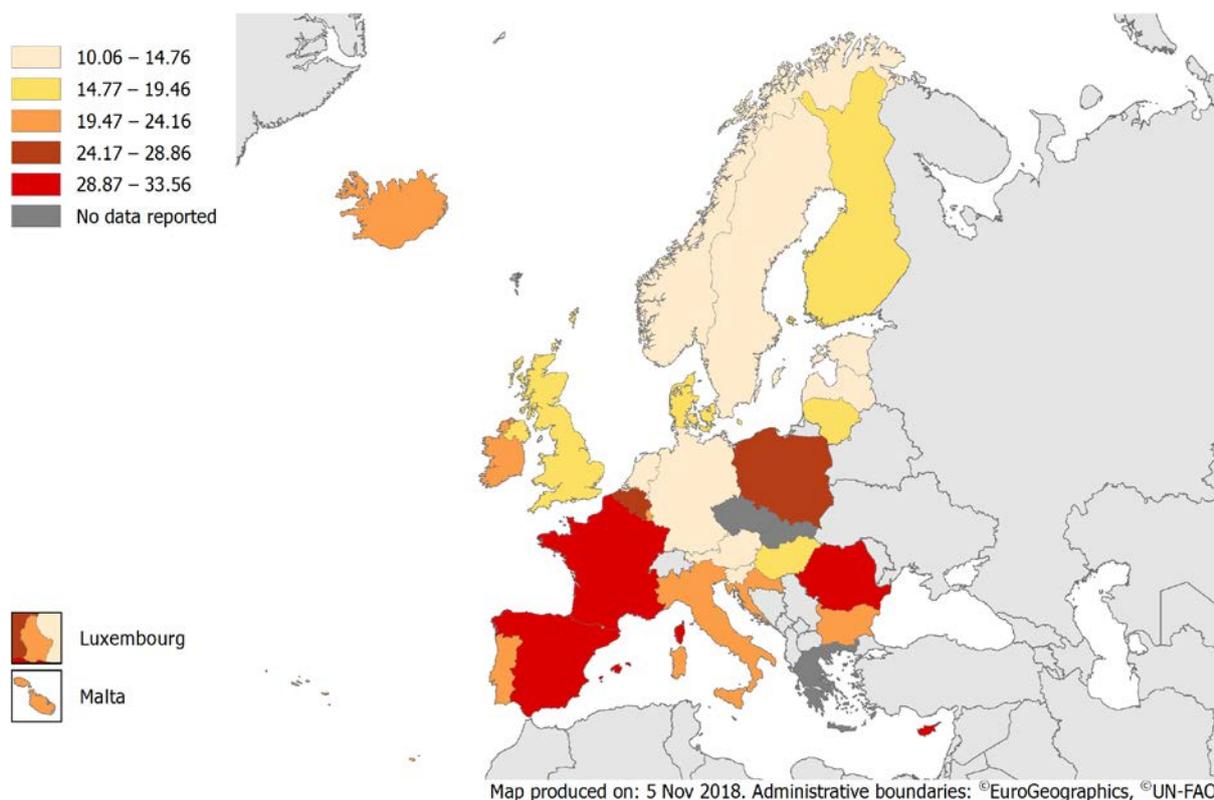
\* Austria, Germany and Iceland only reported community data

EU/EEA: EU/EEA population-weighted mean consumption

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

In 2017, the EU/EEA population-weighted mean consumption of antibacterials for systemic use in the community (i.e. outside hospitals) was 21.8 DDD per 1 000 inhabitants per day, ranging from 10.1 in the Netherlands to 33.6 in Cyprus (Figure 2).

**Figure 2. Consumption of antibacterials for systemic use (ATC group J01) in the community, EU/EEA countries, 2017, expressed as DDD per 1 000 inhabitants per day**



*Cyprus and 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 2017 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 36% (Germany) to 71% (Slovenia) of the total consumption in the community. The proportion of other antibacterial groups varied more widely between countries (e.g. cephalosporins and other beta-lactams (ATC group J01D), from 0.2% (Denmark) to 21% (Germany); macrolides, lincosamides and streptogramins (ATC group J01F), from 5% (Sweden) to 23% (Luxembourg); and quinolone antibacterials (ATC group J01M), from 2% (United Kingdom) to 19% (Cyprus).

**Table 1. Consumption of antibacterials for systemic use (ATC group J01) by country and ATC group level 3 in the community, EU/EEA countries, 2017, expressed as DDD per 1 000 inhabitants per day**

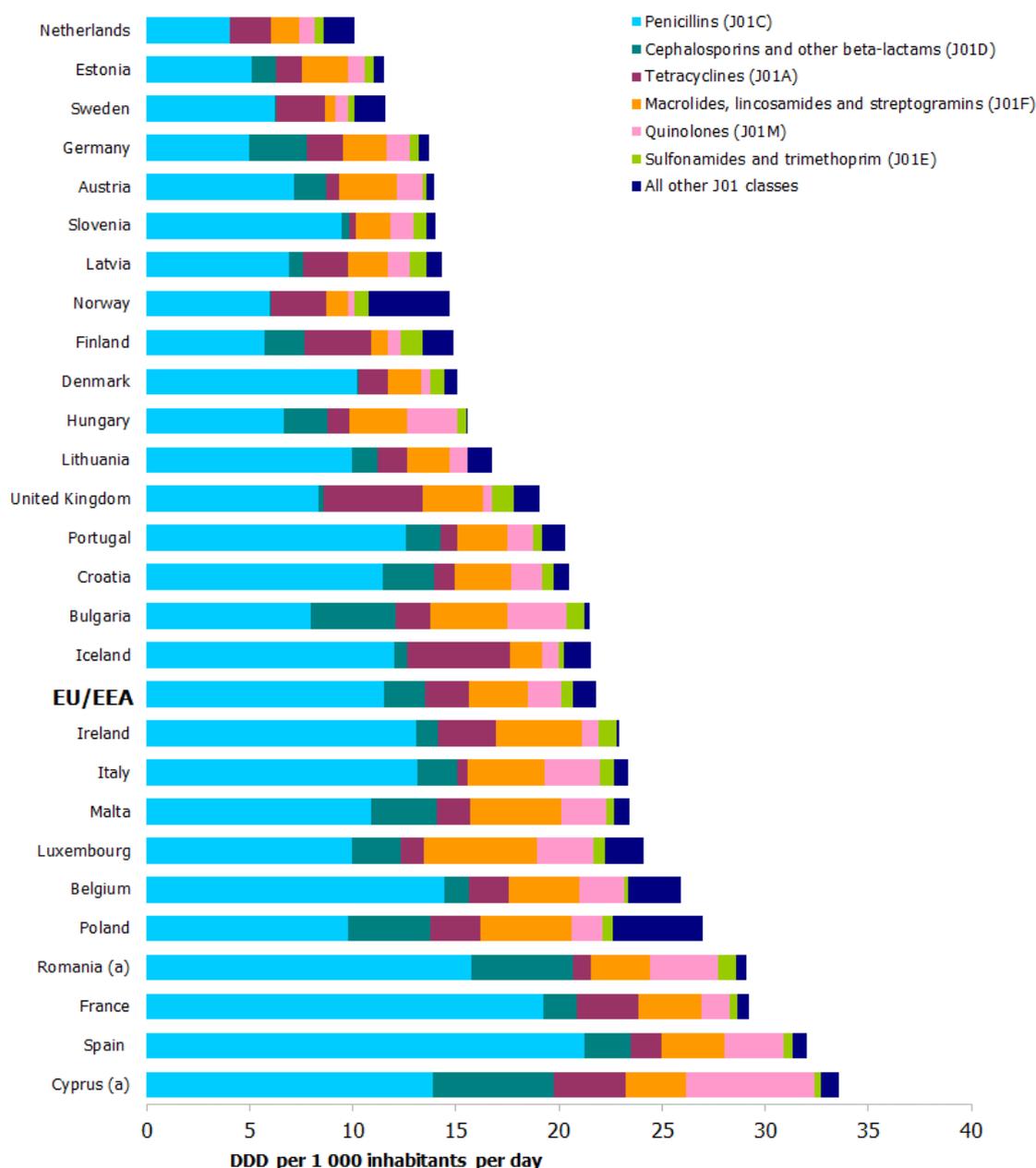
Country	Tetra-cyclines (J01A)	Beta-lactams, penicillins (J01C)	Other beta-lactam antibacterials (J01D)	Sulfonamides and trimethoprim (J01E)	Macrolides, lincosamides and streptogramins (J01F)	Quinolones (J01M)	Other antibacterials (J01X)	Sum (J01B, J01G, and J01R)*	Total (ATC group J01)
Austria	0.6	7.2	1.5	0.2	2.8	1.2	0.4	0.0	14.0
Belgium	1.9	14.5	1.2	0.2	3.4	2.2	2.5	0.0	25.9
Bulgaria	1.6	8.0	4.1	0.8	3.8	2.9	0.1	0.2	21.5
Croatia	1.0	11.5	2.5	0.6	2.7	1.5	0.7	0.0	20.5
Cyprus (a)	3.5	13.9	5.8	0.3	2.9	6.3	0.8	0.1	33.6
Denmark	1.4	10.2	0.0	0.7	1.6	0.4	0.6	0.0	15.0
Estonia	1.3	5.1	1.2	0.4	2.3	0.8	0.5	0.0	11.5
Finland	3.3	5.7	1.9	1.0	0.7	0.7	1.5	0.0	14.9
France	3.0	19.2	1.6	0.4	3.0	1.4	0.5	0.0	29.2
Germany	1.8	5.0	2.8	0.5	2.1	1.1	0.5	0.0	13.7
Hungary	1.1	6.7	2.1	0.4	2.8	2.4	0.1	0.0	15.6
Iceland	5.0	12.0	0.6	0.2	1.6	0.8	1.3	0.0	21.5
Ireland	2.8	13.0	1.1	0.9	4.2	0.8	0.1	0.0	22.9
Italy	0.5	13.1	1.9	0.7	3.8	2.7	0.6	0.1	23.4
Latvia	2.2	6.9	0.7	0.8	2.0	1.0	0.7	0.0	14.3
Lithuania	1.4	9.9	1.3	0.0	2.1	0.9	1.2	0.0	16.8
Luxembourg	1.1	10.0	2.4	0.6	5.5	2.8	1.8	0.1	24.1
Malta	1.6	10.9	3.2	0.4	4.5	2.2	0.4	0.3	23.4
Netherlands	2.0	4.0	0.0	0.4	1.4	0.7	1.5	0.0	10.1
Norway	2.7	6.0	0.1	0.6	1.0	0.4	3.9	0.0	14.7
Poland	2.4	9.8	4.0	0.5	4.5	1.5	4.3	0.0	27.0
Portugal	0.8	12.6	1.6	0.4	2.4	1.3	1.1	0.0	20.3
Romania (a)	0.8	15.7	5.0	0.9	2.9	3.3	0.3	0.2	29.1
Slovenia	0.3	9.4	0.4	0.7	1.7	1.1	0.4	0.0	14.0
Spain	1.5	21.2	2.3	0.4	3.1	2.8	0.5	0.2	32.0
Sweden	2.3	6.2	0.1	0.3	0.5	0.6	1.5	0.0	11.6
United Kingdom	4.8	8.3	0.2	1.0	2.9	0.5	1.3	0.0	19.1
<b>EU/EEA</b>	<b>2.2</b>	<b>11.5</b>	<b>2.0</b>	<b>0.6</b>	<b>2.9</b>	<b>1.6</b>	<b>1.1</b>	<b>0.1</b>	<b>21.8</b>

(a) Cyprus and Romania provided total care data (i.e. including the hospital sector).

\*J01B: Amphenicols; J01G: Aminoglycoside antibacterials; J01R: Combinations of antibacterials

EU/EEA refers to the corresponding population-weighted mean consumption.

**Figure 3. Consumption of antibacterials for systemic use (ATC group J01) by country and ATC group level 3 in the community, EU/EEA countries, 2017, expressed as DDD per 1 000 inhabitants per day**



(a) Cyprus and Romania provided total care data (i.e. including the hospital sector).

EU/EEA refers to the corresponding population-weighted mean consumption.

The EU/EEA population-weighted mean consumption of antibacterials for systemic use decreased from 22.3 DDD per 1 000 inhabitants per day in 2013 to 21.8 in 2017, but there was no statistically significant trend for the five-year period 2013–2017 (Table 2). No countries showed any statistically significant increasing trend for this period. A statistically significant decreasing trend was observed for Finland, Germany, Italy, Luxembourg, the Netherlands, Norway, Sweden and the United Kingdom.

**Table 2.** Trends in consumption of antibacterials for systemic use (ATC group J01) in the community, EU/EEA countries, 2013–2017, expressed as DDD per 1 000 inhabitants per day

Country	2013	2014	2015	2016	2017		Trends in antimicrobial consumption, 2013–2017	Average annual change 2013–2017	Statistically significant trend
Netherlands	10.8	10.6	10.7	10.4	10.1			-0.17	↓
Estonia	11.7	11.7	12.0	11.9	11.5			-0.01	
Sweden	13.0	13.0	12.3	12.0	11.6			-0.38	↓
Germany	15.8	14.6	14.4	14.1	13.7			-0.44	↓
Austria	16.3	13.9	13.9	13.3	14.0			-0.52	
Slovenia	14.5	14.2	14.5	13.9	14.0			-0.34	
Latvia	13.5	12.6	13.3	13.2	14.3			0.22	
Norway	16.2	15.9	15.8	15.2	14.7			-0.37	↓
Finland	18.3	18.1	17.2	16.5	14.9			-0.85	↓
Denmark	16.4	15.9	16.1	15.9	15.0			-0.28	
Hungary	15.5	16.2	17.0	15.4	15.6			-0.05	
Lithuania	18.5	16.0	16.7	16.6	16.8			-0.29	
United Kingdom	20.6	20.8	20.1	19.6	19.1			-0.43	↓
Portugal	19.6	20.3	21.3	21.6	20.3			0.26	
Croatia	21.1	21.4	21.8	20.7	20.5			-0.19	
Bulgaria	19.9	21.2	21.4	19.8	21.5			0.18	
Iceland	21.9*	19.3	19.9	20.7	21.5			N/A	
<b>EU/EEA</b>	<b>22.3</b>	<b>21.9</b>	<b>22.4</b>	<b>22.8</b>	<b>21.8</b>			<b>-0.01</b>	
Ireland	23.7	23.0	25.3	24.2	22.9			-0.03	
Italy	28.6	27.8	27.5	26.9	23.4			-1.14	↓
Malta	23.8	23.7	21.6	21.2	23.4			-0.32	
Luxembourg	27.7	25.8	26.3	25.5	24.1			-0.74	↓
Belgium	27.4	27.2	27.7	27.5	25.9			-0.26	
Poland	23.6	22.8	26.2	24.0	27.0			0.79	
Romania	31.6*	31.2*	33.3*	29.5*	29.1*			-0.67	
France	30.1	29.0	29.9	30.3	29.2			-0.05	
Spain	20.3†	21.6†	22.2†	32.9	32.0			N/A	
Cyprus	28.2*	26.1*	31.1*	32.7*	33.6*			1.73	
Czech Republic	18.9	19.1	19.5					N/A	
Greece	32.2	35.1	36.1	36.3				N/A	
Slovakia	23.6	20.9	24.5	23.6				N/A	

\* Total care data, including the hospital sector.

† Reimbursement data (i.e. not including consumption without a prescription and other non-reimbursed courses).

N/A = not applicable; linear regression was not applied due to missing data, changes in the type of data or changes of sector for which data were reported (community versus total care data) between 2013 and 2017.

The symbol ↓ indicates statistically significant decreasing trends.

EU/EEA refers to the corresponding population-weighted mean consumption.

There were statistically significant decreases in the EU/EEA average five-year trends for consumption of subgroups of antibacterials in the community for tetracyclines and sulphonamides with trimethoprim, while no statistically significant increase is seen for any subgroup of antibacterials.

Trends in consumption of subgroups of antibacterials are available as downloadable tables D1, D2, D3, D4, D5, D6 and D7.

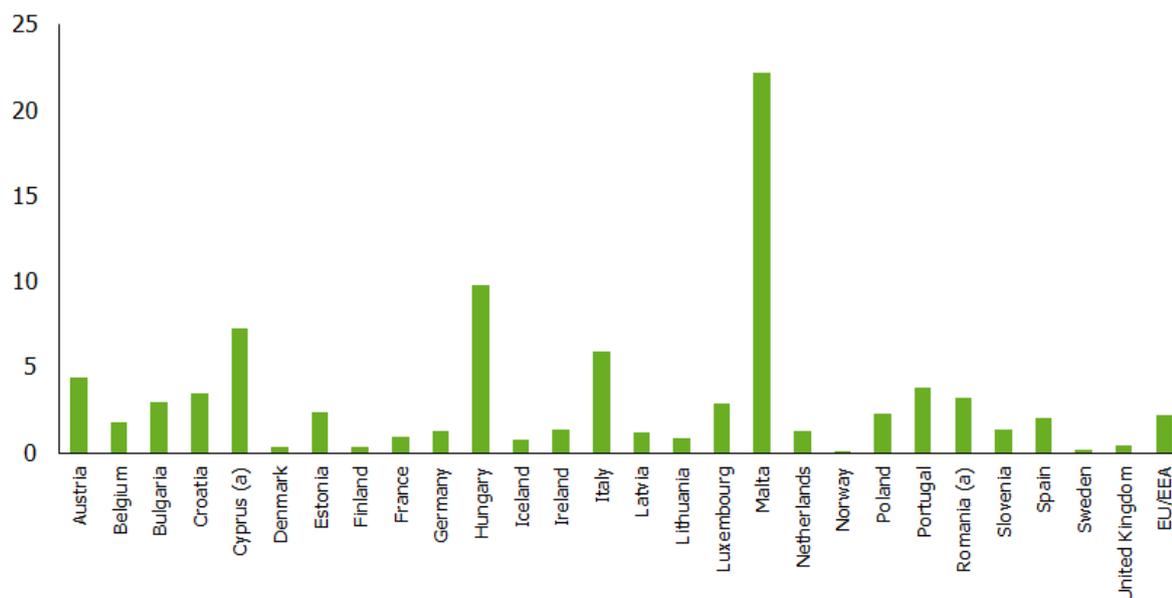
In 2017, 17 countries reported the number of consumed packages of antibacterials for oral use in the community. The consumption of antibacterials for systemic use (ATC group J01, oral administration) in the community ranged from 1.0 package per 1 000 inhabitants per day in Sweden to 4.5 in France (Table D8).

### *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.

The ratio on the EU/EEA level was 2.3 and ranged between countries from 0.1 (Norway) to 22.2 (Malta).

**Figure 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, EU/EEA countries, 2017



(a): Cyprus and Romania provided total care data (i.e. including the hospital sector)

EU/EEA: EU/EEA population-weighted mean consumption (27 countries)

### *ESAC quality indicators for consumption of antibacterials for systemic use (ATC group J01) in the community*

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 ESAC quality indicators - are presented in Table D9 and Figures D2, D3, D5 and D6.

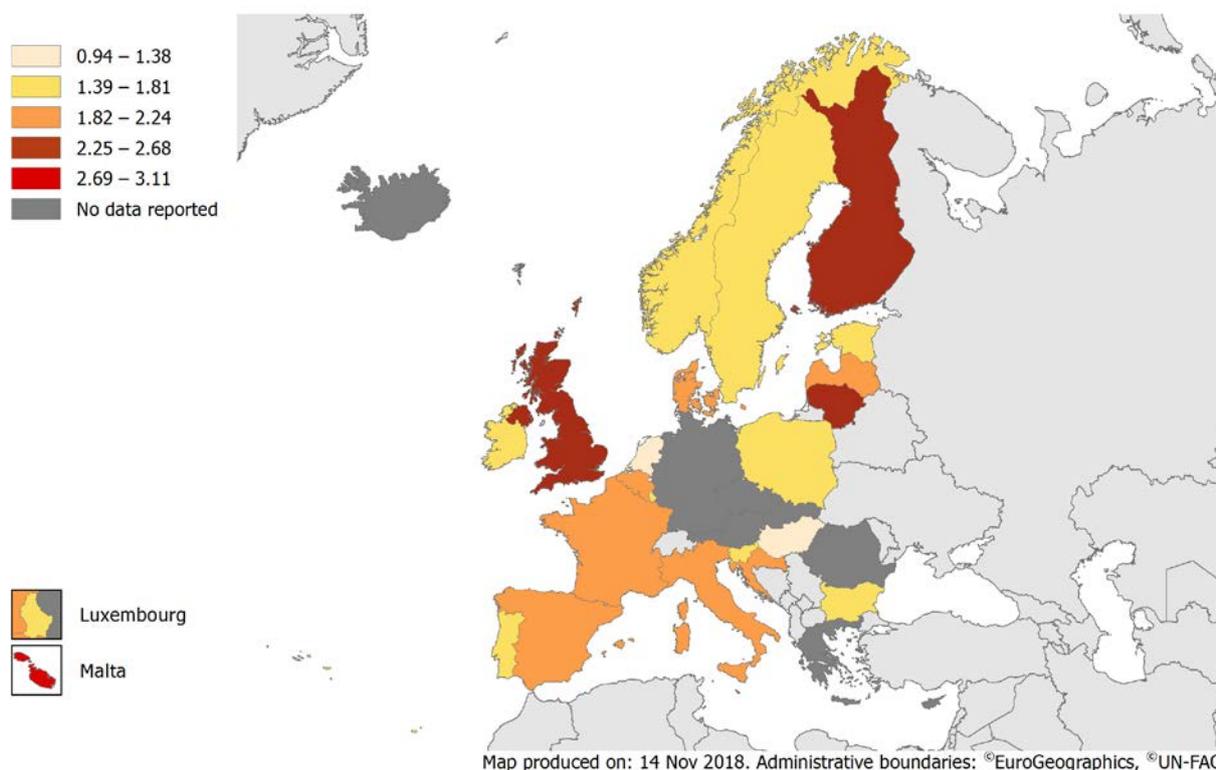
### *Consumption of antibacterials from other ATC groups (A07A, P01A, J04A)*

Twelve 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 24 and 26 countries, respectively (Table D10).

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

In 2017, the EU/EEA population-weighted mean consumption of antibacterials for systemic use in the hospital sector was 2.0 DDD per 1 000 inhabitants per day, ranging from 0.9 in the Netherlands to 3.1 in Malta (Figure 5).

**Figure 5.** Consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, EU/EEA countries, 2017, 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 2017 is presented in Table 3 and Figures 5 and 6. Substantial variations were reported across countries: consumption of cephalosporins and other beta-lactams (ATC group J01D, includes carbapenems) ranged from 7% in the United Kingdom to 59% in Bulgaria; consumption of macrolides, lincosamides and streptogramins (ATC group J01F) from 3% in Lithuania to 13% in Ireland, and consumption of quinolones (ATC group J01M) from 4% in Norway to 18% in Italy.

**Table 3. Consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, by country and ATC group, EU/EEA countries, 2017, expressed as DDD per 1 000 inhabitants per day**

Country	Tetra-cyclines (J01A)	Beta-lactams, penicillins (J01C)	Other beta-lactam antibacterials (J01D)	Sulfon-amides and trimetho-prim (J01E)	Macrolides, lincosamides and strepto-gramins (J01F)	Quino-lones (J01M)	Other antibac-terials (J01X)	Sum (J01B, J01G, and J01R) *	Total (ATC group J01)
Belgium	0.02	0.97	0.40	0.04	0.11	0.19	0.13	0.02	1.89
Bulgaria	0.01	0.13	0.93	0.00	0.11	0.16	0.14	0.11	1.58
Croatia	0.04	0.58	0.59	0.04	0.16	0.27	0.21	0.09	1.98
Denmark	0.04	1.12	0.32	0.12	0.13	0.16	0.14	0.04	2.07
Estonia	0.04	0.60	0.57	0.05	0.16	0.22	0.11	0.04	1.79
Finland (a)	0.16	0.66	0.86	0.08	0.12	0.22	0.14	0.01	2.25
France	0.03	1.22	0.33	0.07	0.12	0.19	0.12	0.05	2.13
Hungary	0.03	0.37	0.36	0.03	0.12	0.22	0.08	0.03	1.24
Ireland	0.04	0.90	0.21	0.02	0.24	0.11	0.18	0.08	1.77
Italy	0.03	0.78	0.41	0.12	0.18	0.40	0.17	0.05	2.14
Latvia	0.11	0.63	0.65	0.07	0.14	0.30	0.22	0.05	2.17
Lithuania	0.05	1.01	0.79	0.00	0.08	0.24	0.24	0.06	2.48
Luxembourg	0.02	0.68	0.54	0.03	0.15	0.21	0.13	0.04	1.78
Malta	0.17	1.54	0.33	0.07	0.33	0.34	0.27	0.07	3.11
Netherlands	0.02	0.41	0.22	0.03	0.06	0.10	0.08	0.04	0.94
Norway	0.07	0.71	0.28	0.06	0.07	0.05	0.09	0.07	1.41
Poland	0.06	0.50	0.65	0.03	0.09	0.21	0.21	0.05	1.79
Portugal (b)	0.02	0.54	0.43	0.07	0.16	0.13	0.17	0.06	1.56
Slovenia	0.02	0.77	0.33	0.05	0.13	0.23	0.11	0.05	1.71
Spain	0.02	0.79	0.50	0.02	0.13	0.36	0.21	0.07	2.10
Sweden	0.18	0.90	0.18	0.04	0.07	0.15	0.08	0.02	1.60
United Kingdom	0.23	1.32	0.18	0.11	0.30	0.11	0.22	0.09	2.55
<b>EU/EEA</b>	<b>0.07</b>	<b>0.90</b>	<b>0.39</b>	<b>0.07</b>	<b>0.16</b>	<b>0.23</b>	<b>0.17</b>	<b>0.08</b>	<b>2.03</b>

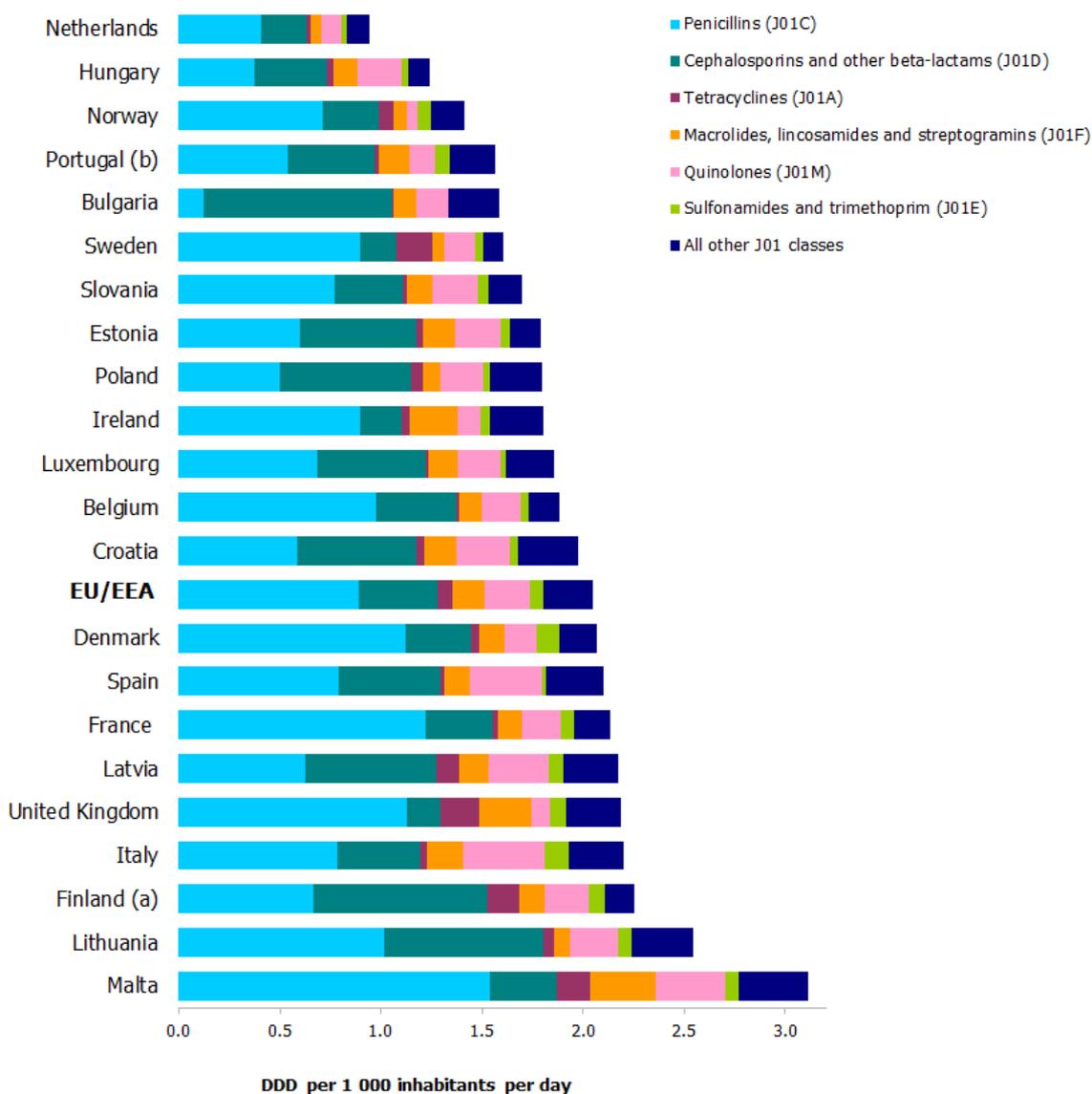
(a) Finland: data include consumption in remote primary healthcare centres and nursing homes.

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

\*J01B: Amphenicols; J01G: Aminoglycoside antibacterials; J01R: Combinations of antibacterials

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

**Figure 6. Consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, by country and ATC group, EU/EEA countries, 2017, expressed as DDD per 1 000 inhabitants per day**



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

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

EU/EEA refers to the corresponding population-weighted mean consumption based on 22 countries that provided data.

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 2013–2017 (Table 4). Statistically significant increasing trends were observed for Croatia and Malta, and a statistically significant decreasing trend was observed for Finland.

**Table 4.** Trends in consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, by country, EU/EEA countries, 2013–2017, expressed as DDD per 1 000 inhabitants per day

Country	2013	2014	2015	2016	2017	Trends in antimicrobial consumption, 2013–2017	Average annual change 2008–2017	Statistically significant trend
Netherlands	1.0	1.0	1.0	1.0	0.9		0.00	
Hungary	1.2	1.2	1.2	1.2	1.2		0.00	
Norway	1.4	1.4	1.4	1.4	1.4		0.00	
Portugal (b)	1.6	1.5	1.6	1.6	1.6		-0.01	
Bulgaria	1.4	1.4	1.4	1.6	1.6		0.06	
Sweden	1.7	1.6	1.7	1.6	1.6		0.00	
Slovenia	1.5	1.6	1.7	1.7	1.7		0.03	
Ireland	1.8	1.6	1.9	1.8	1.8		0.02	
Luxembourg	2.0	1.8	1.8	1.7	1.8		-0.05	
Estonia	1.8	1.8	1.7	1.7	1.8		-0.01	
Poland		1.4	1.4	1.4	1.8		N/A	
Belgium	2.0	1.9	2.0	2.0	1.9		-0.01	
Croatia	1.8	1.9	1.9	1.9	2.0		0.04	↑
<b>EU/EEA</b>	<b>2.0</b>	<b>2.0</b>	<b>2.0</b>	<b>2.1</b>	<b>2.0</b>		0.01	
Denmark	2.0	2.1	2.3	2.0	2.1		-0.01	
Spain					2.1		N/A	
France	2.2	2.2	2.2	2.2	2.1		-0.01	
Italy	2.2	2.1	2.4	2.5	2.1		0.03	
Latvia	2.3	2.2	2.2	2.1	2.2		-0.04	
Finland (a)	2.8	2.6	2.5	2.5	2.3		-0.11	↓
Lithuania	2.4	2.3	2.5	2.6	2.5		0.04	
United Kingdom	2.3	2.5	2.5	2.5	2.5		0.02	
Malta	1.7	2.2	2.8	2.8	3.1		0.33	↑
Greece	2.0	2.1	2.1	2.4			N/A	
Slovakia	2.3	2.5	2.4	2.5			N/A	

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

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

N/A = not applicable; linear regression was not applied due to missing data, between 2013 and 2017.

The symbols ↑ and ↓ indicate statistically significant increasing and decreasing trends, respectively.

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

### 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 2013–2017, as was the case in half of the countries reporting hospital sector data.

In 2017, consumption of carbapenems (ATC group J01DH) was 0.06 DDD per 1 000 inhabitants per day (Table D11). Between 2013 and 2017, the EU/EEA population-weighted mean consumption of carbapenems did not show a statistically significant change (Table D11). A statistically significant increase was observed for nine countries (Bulgaria, Croatia, Cyprus, Estonia, Hungary, Latvia, Lithuania, Malta and Romania). During the period 2013–2017, Italy and Portugal showed a statistically significant decreasing trend.

The EU/EEA population-weighted mean consumption of polymyxins (ATC group J01XB) did not show any statistically significant change during the period 2013–2017 (Table D12). A statistically significant increase was observed for four countries (Hungary, Estonia, Portugal and Italy). During 2013–2017, France and Ireland showed a statistically significant decreasing trend.

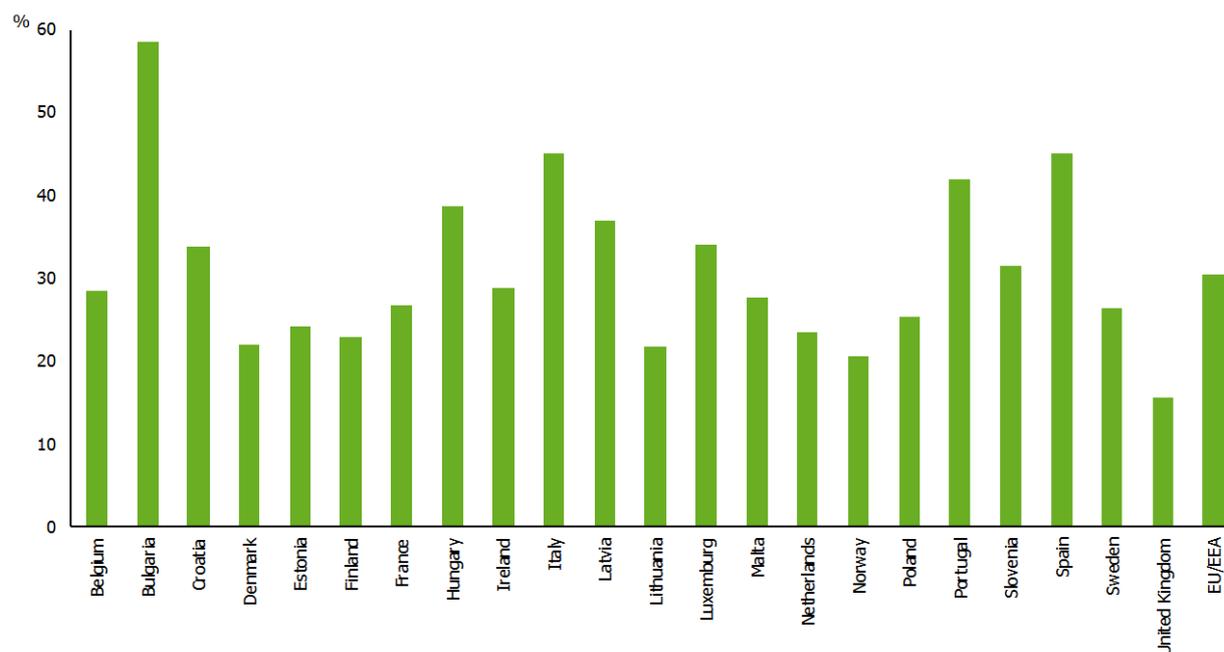
New antibacterial agents (e.g. combinations of cephalosporins and beta-lactamase inhibitors) have recently been authorised for use in the EU. Consumption of such antibacterial agents (ceftazidime-avibactam and ceftolozane-tazobactam) was very low in 2017 and only reported by eight countries.

### *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 Figure 7.

The EU/EEA proportion was 30% and ranged from 16% (United Kingdom) to 59% (Bulgaria).

**Figure 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, EU/EEA countries, 2017**



EU/EEA: EU/EEA population-weighted mean consumption (22 countries)

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

In 2017, hospital consumption of oral vancomycin (ATC A07AA09) and fidaxomicin (ATC A07AA12) was reported from fourteen 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 2017, 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.

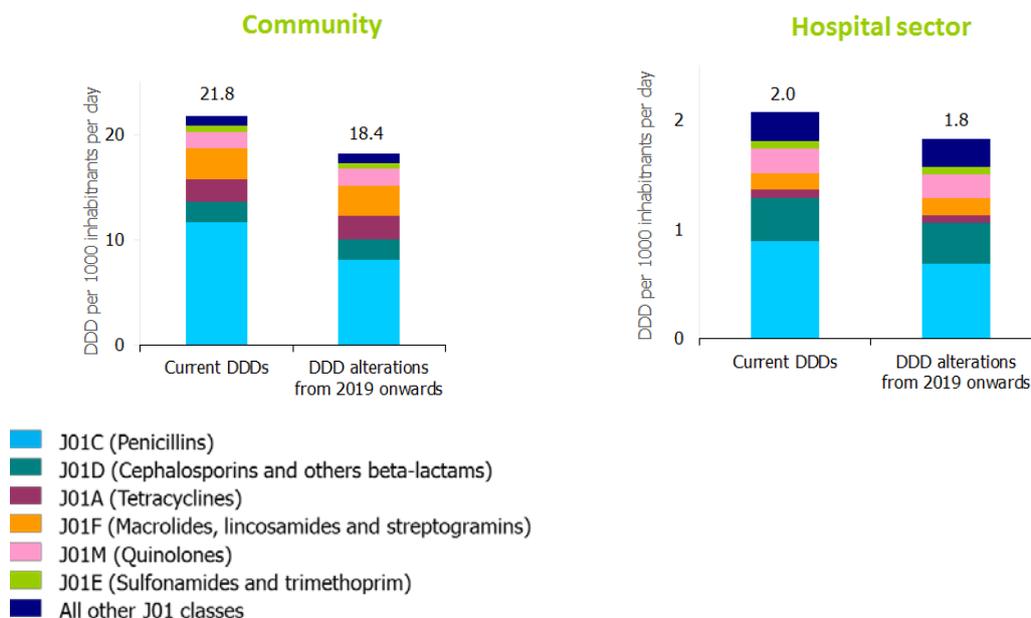
### **Impact of 2019 DDD alterations on the calculated consumption of antibacterials for systemic use**

The EU/EEA population-weighted mean consumption of antibacterials for systemic use in the community in 2017, applying the ATC Index with DDDs 2018, was 21.7 DDD per 1 000 inhabitants per day. When applying the ATC Index with DDDs 2019 (valid from 1 January 2019 onwards), it was 18.4 DDD per 1 000 inhabitants per day.

The pattern of consumption of antibacterials for systemic use calculated with DDDs for 2018 and 2019 is presented in Figure D8.

In the community, penicillins accounted for 53% of antibacterials consumed for systemic use when the ATC Index with DDDs 2018 was used and for 43% when the ATC Index with DDDs 2019 was used. In the hospital sector, penicillins accounted for 44% consumption of antibacterials for systemic use when the ATC Index with DDDs 2018 was used and for 38% when the ATC Index with DDDs 2019 was used.

**Figure 8. Comparison of calculated consumption of antibacterials for systemic use (ATC group J01) with the current DDDs and new DDD alterations, EU/EEA population weighted-mean, in the community (left) and in the hospital sector (right), 2017, expressed as DDD per 1 000 inhabitants per day**



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

In 2017, 25 countries reported data on consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01B) in the community (Table D14 and Figure D7).

The EU/EEA population-weighted mean consumption was 0.9 DDD per 1 000 inhabitants per day. The consumption varied by a factor of 8, ranging from 0.38 (Croatia) to 3.0 DDD per 1 000 inhabitants per day (Belgium).

In 2017, 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 2017, 19 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 0.08 DDD per 1 000 inhabitants per day. Consumption varied by a factor of six, from 0.03 (Bulgaria) to 0.19 DDD per 1 000 inhabitants per day (Denmark).

In 2017, fluconazole (J02AC01) accounted for 53% 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 33% (Malta) to 94% (Bulgaria).

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

Twenty-five countries reported data on antivirals for systemic use (ATC group J05) in 2017. The data are pooled across the two sectors (Table D16). Austria, Germany, Iceland, and the Netherlands reported only data on consumption of antivirals for systemic use (ATC group J05) in the community.

The total EU/EEA population-weighted mean consumption of antivirals for systemic use (ATC group J05) for countries reporting both sectors was 1.97 DDD per 1 000 inhabitants per day. Country-specific consumption showed a 31-fold difference from 0.22 (Spain) to 6.91 (Portugal) DDD per 1 000 inhabitants per day.

The EU/EEA population-weighted mean consumption in the reporting countries was highest for combinations of antivirals to treat HIV infections (ATC group J05AR) (0.64 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', 'herpes antivirals', 'influenza antivirals' and one group for remaining substances. The EU/EEA population-weighted mean consumption of HIV/AIDS antivirals accounted for 54% 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 0.6% (Poland) to 87% (Portugal).

Malta reported the highest proportion of HIV/hepatitis B antivirals consumed (45%) and Slovenia reported the highest proportion of hepatitis B antivirals consumed (28%).

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 0.3% (Malta) to 13% (Lithuania). In 2017, direct-acting antivirals (DAA) were under surveillance within this group and 23 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 100% (Spain).

In 2017, the EU/EEA population-weighted mean consumption of substances used to treat influenza (rimantadine, J05AC02; zanamivir, J05AH01; oseltamivir, J05AH02) was 0.03 DDD per 1 000 inhabitants per day. The consumption ranged from <0.001 DDD per 1 000 inhabitants per day in Luxembourg, where it accounted for 0.01% of the total consumption of antivirals for systemic use (ATC J05), to 0.17 DDD per 1 000 inhabitants per day in Latvia and Lithuania, accounting for 26% of the total consumption of antivirals for systemic use. Lithuania reported the highest proportion of anti-influenza substances consumed (26%).

## Discussion

Reducing unnecessary and inappropriate use of antimicrobials has become a public health priority in an attempt to control increasing antimicrobial resistance, both in the community and in the hospital sector. Coordinated interventions designed to measure and improve the use of antimicrobials are the main elements of antimicrobial stewardship programmes at all levels.

Each year, EU/EEA countries report antimicrobial consumption data to ESAC-Net and these data are instrumental for the evaluation of such stewardship interventions at national and international level. Effective antimicrobial stewardship programmes should have developed tools to measure both the quantity and quality of antimicrobial use.

The 'Driving re-investment in Research & Development (R&D) and responsible antibiotic use' project (DRIVE-AB), a public-private consortium funded by the EU Innovative Medicines Initiative (IMI), has proposed quantity metrics and quality indicators for antibiotic use [5,6]. These quantity metrics and quality indicators are intended to be adapted to local settings – i.e. they should be feasible, valid and reliable for the specific country or region in question. Broadly accepted metrics (ATC/DDD methodology) that have been used in this report are also proposed by the DRIVE-AB project.

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. 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 jointly establish a list of harmonised outcome indicators for antimicrobial consumption and antimicrobial resistance. The chosen indicators had to take the 'One Health' approach into account and be suitable for evaluating progress made in reducing bacterial resistance to key antimicrobials in humans and animals. They also had to be able to evaluate improvements in the appropriateness and need for the use of antimicrobials in the EU. It is intended that the indicators should be reconsidered at least every five years to determine whether they still reflect the data available [7].

The primary antimicrobial consumption indicator – i.e. 'DDD per 1 000 inhabitants per day' – has been used in this and previous ESAC-Net reports. The two secondary outcome indicators, one for community consumption and the other for consumption in the hospital sector, are reported for the first time in this ESAC-Net report.

The quality of antimicrobial consumption data depends on the type of data available for a given sector. For ESAC-Net, countries provide sales or/and reimbursement data that each have 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, type (source) of data in individual countries may change from one year to another, possibly affecting the results of patterns and trends in antimicrobial drug consumption.

The indicator 'packages per 1 000 inhabitants per day' has disadvantages and there are concerns about its suitability for making country comparisons [13]. It may be useful as an additional metric for longitudinal monitoring of antibiotic consumption only at national level, provided that the average number of packages (of the same size and unit strength) per prescription is one. If used as a surrogate for prescriptions it can assess the effectiveness of antibiotic awareness campaigns. However, when more than one package may be prescribed per encounter, this indicator becomes unreliable if used as the sole metric.

For international benchmarking, the indicator 'DDD per 1 000 inhabitants per day', although not perfect, remains preferable. Reporting consumption in DDDs overcomes the limitations of packages, such as differences in prescribing regulations, the number of items or dose per item of an antibiotic in a package. Moreover, if assessing the 'antibiotic pressure', DDDs are more appropriate than packages or prescriptions.

In 2017, 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 [13].

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 2013–2017. In contrast to previous years, no country showed a statistically significant increasing five-year trend an increasing number of countries reported a statistically significant decreasing five-year trend in the consumption of antibacterials for systemic use - eight countries in this report compared to four countries in the last report. In addition, no statistically significant increasing trend of EU/EEA population-weighted mean consumption of any group of antibacterials and a

statistically significant decreasing trend was even observed for tetracyclines (J01A) and sulfonamides and trimethoprim (J01E). Twelve countries reported a statistically significant decreasing trend in the consumption of tetracyclines and ten countries in the consumption of sulphonamides and trimethoprim. These five-year trends in the consumption of antibacterials for systemic use in the community may reflect antimicrobial stewardship activities, including awareness campaigns, in EU/EEA countries.

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. For the EU/EEA in 2017 it was 8.0 DDD per person per year. In other words, on average in 2017 each EU citizen was treated with an antibiotic for approximately eight days, which in most cases corresponds to one antibiotic course per year.

Any ranking of the countries based on ESAC quality indicators should be interpreted with caution, as the indicators are not independent – e.g. 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 macrolides. For countries where changes in the ranking suggest quality improvement, this may reflect a relative change compared to other countries. For example, quality may have decreased in all countries but less so in the specific country in question [15]. It should be emphasised that these indicators cannot by themselves indicate quality of antimicrobial use, unless they are combined with corresponding clinical data (e.g. resistance pattern, indications, current national programmes such as guidelines, restrictions). The types of healthcare facilities included in the hospital sector differ across EU/EEA countries. For example, hospital data from Finland include consumption from nursing homes and remote primary healthcare centres. For this reason, antimicrobial consumption from the hospital sector in Finland should be interpreted with caution when compared with that of other countries. The same is true for Malta and the United Kingdom. For example, the true national consumption of antimicrobials in Malta, in both sectors could be affected by the number of tourists that may contribute to the total antimicrobial consumption<sup>1</sup>. In the United Kingdom, on average, patients have shorter lengths of hospital stay than in other EU countries and there is a policy of dispensing a full course of antimicrobials for patients discharged from the hospital via the hospital pharmacy.

In contrast to prescribing practices in the community, penicillins were not the most frequently prescribed antibacterial subclass in the hospital sector for all countries, and the proportions of cephalosporins, other beta-lactams (including carbapenems) and other groups of antimicrobials were generally higher than in the community. The appropriateness of consumption needs to be assessed at a national level.

Inappropriate antibacterial prescribing in hospitals promotes the emergence and spread of multidrug-resistant (MDR) bacteria responsible for healthcare-associated infections and is becoming a global healthcare issue [16,17]. The prevalence of antibiotic-resistant microorganisms, 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 gram-negative 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 MDR 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 [16,18].

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 [16]. 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 in providing guidance for alternative treatments. This shortage could have caused a shift towards increased consumption of third- and fourth-generation cephalosporins and of carbapenems, but this would need to be assessed at national level in EU/EEA countries. In 2017, the EU/EEA population-weighted mean consumption of

<sup>1</sup> [https://nso.gov.mt/en/News\\_Releases/View\\_by\\_Unit/Unit\\_C3/Tourism\\_Statistics/Documents/2017/News2017\\_106.pdf](https://nso.gov.mt/en/News_Releases/View_by_Unit/Unit_C3/Tourism_Statistics/Documents/2017/News2017_106.pdf)

piperacillin-tazobactam still showed a statistically significant increasing trend, as was the case in 11 out of 20 countries that reported consumption of piperacillin-tazobactam, compared to 17 out of 21 countries in 2016.

Nine countries reported a statistically significant increasing trend in carbapenem consumption, but these increases did not affect the EU/EEA population-weighted mean consumption in the past five years. For polymyxins, the EU/EEA population-weighted mean consumption did not show any statistically significant trend, but statistically significant increasing consumption trends were observed for a smaller number of countries (four in 2017) than in 2016 (nine countries).

This finding is consistent with the 2017 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* isolates from invasive infections has been stable in recent years [20].

Assuming that the average duration of carbapenem treatment is ten days, the consumption of 0.06 DDD per 1 000 inhabitants per day corresponds to more than one million carbapenem treatment courses administered in the EU/EEA each year.

As expected, the consumption pattern of antimycotics and antifungals for systemic use in the hospital sector differed to that in the community due to different aetiology and variations in the diseases and disease severity treated in the sectors. In the hospital sector for the EU/EEA, the prevailing agent 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. An increasing number of countries are reporting consumption of DAAs 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 this variation.

The alterations in DDDs for eight antibacterial agents that will come into force from 1 January 2019 better reflect the doses used in clinical practice than those listed in the ATC Index with DDDs 2018. When applying the ATC Index with DDDs 2019, the EU/EEA population-weighted mean consumption of antibacterials for systemic use in the community appears to be 15% lower, and in the hospital sector 14% lower than when applying the ATC Index with DDDs 2018. Application of the new DDDs has the largest impact on consumption of penicillins. The changes in DDDs will impact the ranking of countries when making international comparison of the pattern and extent of consumption. However, trends for individual countries will not be affected provided that the same DDDs are applied throughout the data set.

## Public health conclusions

Antimicrobial resistance is a serious threat to public health and antimicrobial consumption is one of the main drivers of resistance. Antimicrobial stewardship refers to a set of coordinated strategies to improve antimicrobial use in order to prevent emergence of resistance and improve patient outcomes. It includes continuous monitoring of bacterial 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 Europe requires reliable national antimicrobial consumption data.

Excessive antibiotic use in hospitals promotes the emergence and spread of MDR bacteria responsible for healthcare-associated infections. Carbapenem use creates selective pressure for the development of carbapenem resistance, which is currently the greatest antibiotic resistance threat. The use of alternative antibacterials rather than carbapenems might reduce the selective pressure for emergence and selection of carbapenem-resistant MDR gram-negative bacteria.

Although there was no statistically significant trend in the consumption of last-line groups of antimicrobials, such as carbapenems and polymyxins, several EU/EEA countries showed a statistically significant increasing trend in the consumption of these last-line antimicrobials, which should be an indication that stronger stewardship measures are required in those countries.

Responsible use of antimicrobials, especially broad-spectrum and last-line antimicrobials, should be a high priority of national antimicrobial stewardship programmes.

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## Annex

**Annex 1.** Further sub-classification of macrolides, quinolones and antivirals