SURVEILLANCE REPORT

Annual Epidemiological Report for 2015

Antimicrobial consumption

Key facts

- Thirty countries, including all EU Member States and two EEA countries (Iceland and Norway) reported antimicrobial consumption for the community, i.e. outside hospitals, and 23 countries reported data for the hospital sector in 2015.
- In the community, the average consumption of antibacterials for systemic use (Anatomical Therapeutic Chemical (ATC) group J01) was 22.4 DDD per 1 000 inhabitants per day (country range: 10.7–36.1). During the period 2011–2015, there was no statistically significant change. However, a statistically significant decreasing trend was observed for Finland, the Netherlands and Sweden.
- The average consumption of antimycotics and antifungals for systemic use (ATC groups J02 and D01BA) in the community was 0.96 DDD per 1 000 inhabitants per day (country range: 0.34–3.1).
- In the hospital sector, the average consumption of antibacterials for systemic use was 2.0 DDD per 1 000 inhabitants per day (country range: 1.0–2.9) and did not show any statistically significant change during the period 2011–2015.
- The average consumption of carbapenems was 0.05 DDD per 1 000 inhabitants per day (country range: 0.02–0.14) and there was no statistically significant change between 2011 and 2015. However, a statistically significant increasing trend was observed for five countries.
- The average consumption of polymyxins was 0.015 DDD per 1 000 inhabitants per day (country range: <0.001–0.095) and did not show any statistically significant change during the period 2011–2015. However, a statistically significant increasing trend was observed for eight countries.
- The average consumption of antimycotics and antifungals for systemic use (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) in 2015 was 2.7 DDD per 1 000 inhabitants per day (country range: 0.59-5.5).

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Stockholm, June 2018

Methods

This report is based on data for 2015 retrieved from The European Surveillance System (TESSy) on 19 February 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 [1].

An overview of the national surveillance systems is available online [2].

A subset of the data used for this report is available through ECDC's online *Surveillance atlas of infectious diseases* [3].

This surveillance report is based on antimicrobial consumption surveillance data collected through the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) for 2015.

The European Surveillance of Antimicrobial Consumption Network (ESAC-Net) reports to the EU/EEA surveillance system for antimicrobial consumption in humans. This is done via the European Surveillance System (TESSy), the ECDC platform for collecting, analysing and disseminating surveillance data regarding infectious diseases in Europe.

All 28 EU Member States and two EEA countries (Iceland and Norway) report antimicrobial consumption data at the European level. The data shown in this report were extracted from the TESSy database as of 19 February 2018.

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 with DDDs 2016 were used [4]. One DDD is the assumed to be the average maintenance dose per day for a drug used in its main indication for adults. It is a technical unit of measurement, not a standard for appropriate daily dosing. Application of ATC/DDD methodology allows the aggregation of different brands of medicines with different pack sizes and different strengths into units of measurement of active substances. It is an internationally accepted standard for undertaking valid and reliable cross-national and longitudinal studies of drug utilisation, provided its limitations are taken into account.

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 for oral administration is classified as an intestinal anti-infective in the group A07A, metronidazole for oral administration as an agent against amoebiasis and other protozoal diseases in the group P01A. Both drugs are also used in the indication of *Clostridium difficile* infections. Rifampicin is classified as a drug for the treatment of tuberculosis (J04A). In clinical practice rifampicin is also used in *Haemophilus influenzae* infections or in combination with other antibacterials to treat 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. Consumption data on antivirals for systemic use are presented as aggregate numbers for both the community and the hospital sector.

Although the ATC/DDD methodology recommends presenting hospital consumption as the number of DDDs per 100 bed-days [4], this report uses DDD per 1 000 inhabitants per day for both the community and the hospital sector because currently denominator data on the total number of occupied bed-days are not available for most EU/EEA countries. In addition, presentation of data with the same denominator enables cross-sectorial comparison.

For antibacterial consumption in the community, the report uses an additional indicator - 'packages per 1 000 inhabitants per day' for those countries which provided data on the number of packages consumed, in accordance with the ATC index. This indicator only considers orally administered antibacterials, which represent most of the antibacterials for systemic use consumed in the community. It does not take into account dosage information. 'Packages per 1 000 inhabitants per day' may be used as a proxy for the number of prescriptions, provided that one antibiotic package is prescribed per prescription encounter.

In addition to presenting the pattern of antimicrobial consumption, consensus-based ESAC quality indicators, published in 2007 by the ESAC project were used to better describe antimicrobial consumption [5].

Consumption displayed with the label 'EU/EEA mean' is based on 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 or packages 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 were assessed using linear regression.

More details on the collection and validation of European antimicrobial consumption data are available in the ESAC-Net report and ESAC-Net reporting protocol which can be found on the ECDC website [6, 7].

Antimicrobial consumption

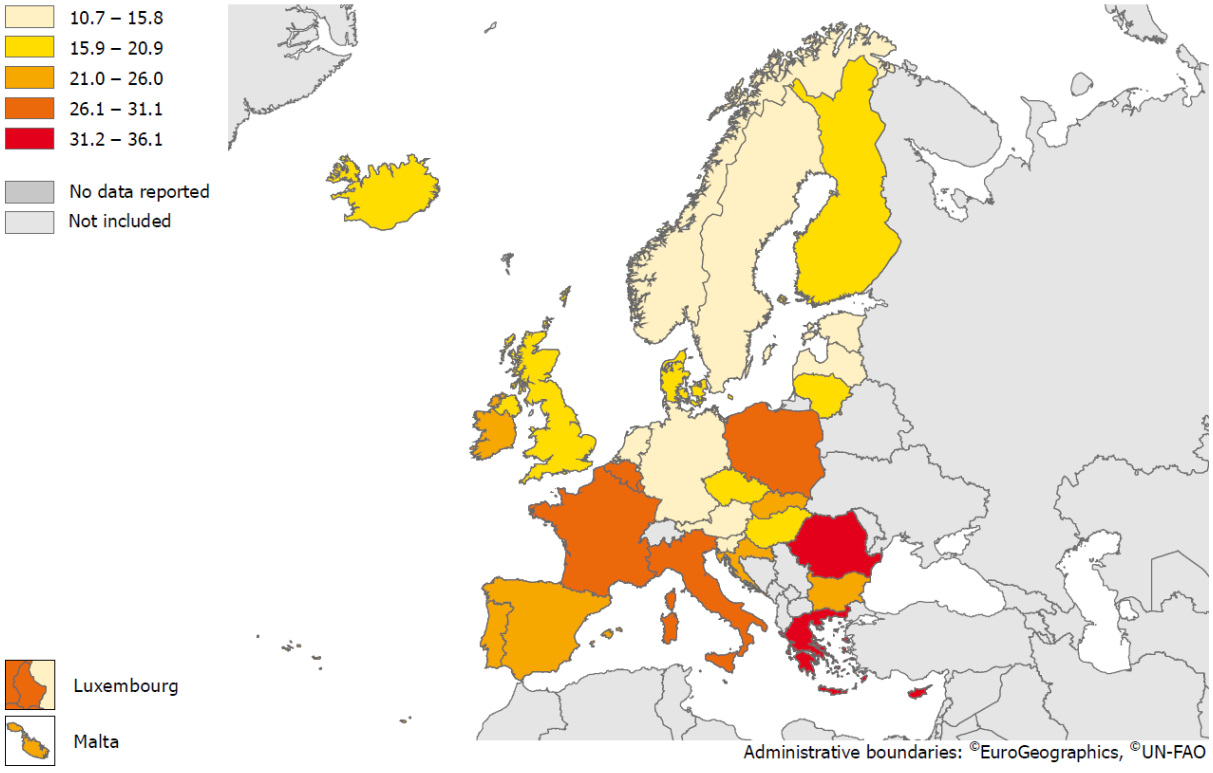
Thirty countries, including all EU Member States and two EEA countries (Iceland and Norway) reported antimicrobial consumption for the community sector and 23 countries reported consumption for the hospital sector in 2015. Two countries (Cyprus and Romania) reported data on total consumption in the country – i.e. without differentiating between the community and the hospital sector. 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. Luxembourg changed the type of data for the hospital sector from reimbursement to sales data.

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

Indicator: DDD per 1 000 inhabitants per day

In 2015, EU/EEA population-weighted mean consumption of antibacterials for systemic use in the community (i.e. outside hospitals) was 22.4 DDD per 1 000 inhabitants per day, ranging from 10.7 in the Netherlands to 36.1 in Greece (Figure 1).

Figure 1. Consumption of antibacterials for systemic use (ATC group J01) in the community, EU/EEA, 2015, expressed as DDD per 1 000 inhabitants per day



Cyprus and Romania provided total care data - i.e. including the hospital sector.

Spain provided reimbursement data - i.e. not including consumption without a prescription and other non-reimbursed courses.

Consumption of major subgroups of antibacterials for systemic use (ATC group J01) in the community in 2015 is presented in Table 1 and Figure 2. As in previous years, penicillins (ATC group J01C) were the most frequently used antibacterials in all countries, ranging from 32% (Germany) to 66% (Denmark and Slovenia) of the total consumption in the community, whereas 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 22%

(Germany); macrolides, lincosamides and streptogramins (ATC group J01F), from 5% (Sweden) to 25% (Slovakia); and quinolones (ATC group J01M), from 2% (United Kingdom) to 16% (Hungary).

Table 1. Consumption of antibacterials for systemic use (ATC group J01) and ATC group level 3 in the community, EU/EEA, 2015, expressed as DDD per 1 000 inhabitants per day

Country	Tetra-cyclines (J01A)	Beta-lactams, penicillins (J01C)	Other beta-lactam antibac-terials (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)
Austria	1.0	6.6	1.4	0.2	3.1	1.3	0.3	0.0	14.0
Belgium	2.0	16.5	1.5	0.2	3.7	2.6	2.8	0.0	29.3
Bulgaria	1.7	8.2	3.9	0.8	3.8	2.8	0.0	0.2	21.4
Croatia	1.1	11.9	2.7	0.6	3.1	1.5	0.8	0.0	21.8
Cyprus (a)	3.6	13.3	5.3	0.2	3.3	4.6	0.7	0.1	31.1
Czech Republic	2.0	8.3	2.2	0.9	4.0	0.9	1.1	0.1	19.5
Denmark	1.6	10.7	0.0	0.7	1.8	0.5	0.7	0.0	16.1
Estonia	1.4	4.8	1.2	0.4	2.4	0.9	0.8	0.0	12.0
Finland	3.9	6.3	2.1	1.3	1.0	0.7	1.8	0.0	17.2
France	3.3	18.8	2.1	0.4	3.2	1.6	0.5	0.0	29.9
Germany	2.0	4.5	3.1	0.5	2.4	1.3	0.5	0.0	14.4
Greece	2.6	14.6	7.6	0.4	7.5	2.7	0.8	0.1	36.1
Hungary	1.2	7.1	2.0	0.5	3.3	2.7	0.2	0.0	17.0
Iceland	4.6	10.7	0.5	0.6	1.7	0.9	1.0	0.0	19.9
Ireland	2.6	15.5	1.2	1.1	4.2	0.9	0.1	0.0	25.6
Italy	0.5	15.5	2.3	0.3	4.6	3.4	0.7	0.1	27.5
Latvia	2.2	6.5	0.5	0.8	1.8	1.1	0.3	0.0	13.3
Lithuania	1.3	9.6	1.2	0.4	1.9	0.9	1.4	0.0	16.7
Luxembourg	1.7	13.4	3.5	0.3	3.6	2.5	1.3	0.0	26.3
Malta	0.8	8.8	4.2	0.2	4.1	2.7	1.1	0.3	22.2
Netherlands	2.3	4.4	0.0	0.4	1.4	0.8	1.5	0.0	10.7
Norway	3.1	6.4	0.1	0.7	1.3	0.5	3.7	0.0	15.8
Poland	2.4	10.4	2.9	0.6	4.6	1.4	3.9	0.0	26.2
Portugal	0.8	12.2	1.6	0.4	3.1	2.0	1.1	0.0	21.3
Romania (a)	1.1	18.8	5.3	0.9	3.2	3.5	0.2	0.4	33.3
Slovakia	1.7	8.9	4.7	0.4	6.2	2.4	0.1	0.0	24.5
Slovenia	0.4	9.6	0.3	0.8	1.9	1.2	0.4	0.0	14.5
Spain (b)	0.7	14.5	1.6	0.3	2.3	2.3	0.5	0.0	22.2
Sweden	2.5	6.3	0.1	0.4	0.6	0.7	1.6	0.0	12.3
United Kingdom	5.0	8.9	0.3	1.3	3.1	0.5	1.0	0.0	20.1
EU/EEA	**2.2**	**11.4**	**2.2**	**0.6**	**3.2**	**1.7**	**1.0**	**0.0**	**22.4**

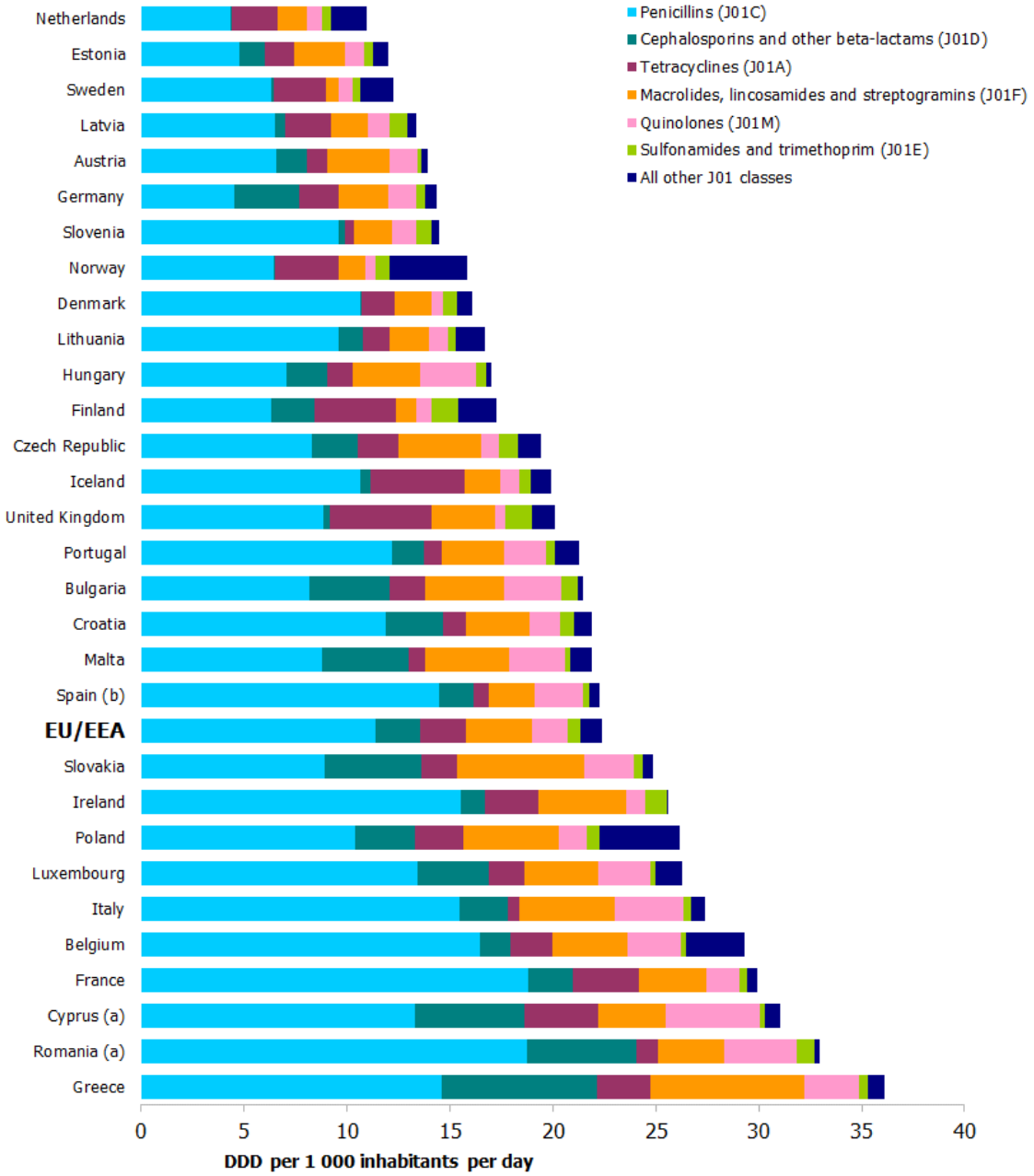
(a) Cyprus and Romania provided total care data (i.e. including the hospital sector).

(b) Spain provided reimbursement data - i.e. not including consumption without a prescription and other non-reimbursed courses.

**J01B: amphenicols; J01G: aminoglycoside antibacterials; J01R: combinations of antibacterials*

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

Figure 2. Consumption of antibacterials for systemic use (ATC group J01) and ATC group level 3 in the community, EU/EEA, 2015, expressed as DDD per 1 000 inhabitants per day



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

(b) Spain provided reimbursement data, i.e. not including consumption without a prescription and other non-reimbursed courses.

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

The EU/EEA population-weighted mean consumption increased from 21.6 DDD per 1 000 inhabitants per day in 2011 to 22.4 in 2015, but there was no statistically significant trend (Table 2). No country showed a statistically significant increasing trend for this period. However, a statistically significant decreasing trend was observed for Finland, the Netherlands and Sweden.

Table 2. Trends in consumption of antibacterials for systemic use (ATC group J01) in the community, EU/EEA, 2011–2015, expressed as DDD per 1 000 inhabitants per day

Country	2011	2012	2013	2014	2015	Trends in antimicrobial consumption, 2011–2015	Average annual change 2011–2015	Statistically significant trend
Netherlands	11.4	11.3	10.8	10.6	10.7		-0.21	↓
Estonia	12.2	11.7	11.7	11.7	12.0		-0.04	
Sweden	14.3	14.1	13.0	13.0	12.3		-0.51	↓
Latvia	12.8	13.0	13.5	12.6	13.3		0.06	
Austria	14.5	14.0	16.3	13.9	14.0		-0.12	
Germany	14.1	14.9	15.8	14.6	14.4		0.07	
Slovenia	14.4	14.3	14.5	14.2	14.5		0.01	
Norway	16.5	16.9	16.2	15.9	15.8		-0.24	
Denmark	17.4	16.4	16.4	15.9	16.1		-0.32	
Lithuania	19.0*	16.2	18.5	16.0	16.7		N/A	
Hungary	15.9	15.0	15.5	16.2	17.0		0.33	
Finland	20.1	19.5	18.3	18.1	17.2		-0.71	↓
Czech Republic	18.4	17.5	18.9	19.1	19.5		0.39	
Iceland	22.3*	22.1*	21.9*	19.3	19.9		N/A	
United Kingdom		20.1	20.6	20.8	20.1		N/A	
Portugal	23.2	22.7	19.6†	20.3†	21.3†		N/A	
Bulgaria	19.5	18.5	19.9	21.2	21.4		0.67	
Croatia	19.4	21.7	21.1	21.4	21.8		0.45	
Malta	23.4	22.5	23.8	23.7	22.2		-0.14	
Spain	20.9†	19.7†	20.3†	21.6†	22.2†		0.47	
EU/EEA	**21.6**	**21.7**	**22.3**	**21.9**	**22.4**		**0.18**	
Slovakia	23.8*	20.0	23.6	20.9	24.5		N/A	
Ireland	22.6	23.0	23.8	23.1	25.6		0.60	
Poland	22.1†	22.9	23.6	22.8	26.2		N/A	
Luxembourg	27.8	27.7	27.7	25.8	26.3		-0.48	
Italy	28.2	27.5	28.6	27.8	27.5		-0.12	
Belgium	29.0	29.8	29.6	28.5	29.3		-0.07	
France	28.7	29.7	30.1	29.0	29.9		0.18	
Cyprus	32.0*	29.7*	28.2*	26.1*	31.1*		-0.55	
Romania	30.9*	30.4*	31.6*	31.2*	33.3*		0.56	
Greece	35.7	32.5	32.2	35.1	36.1		0.34	

** 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 2011 and 2015.

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

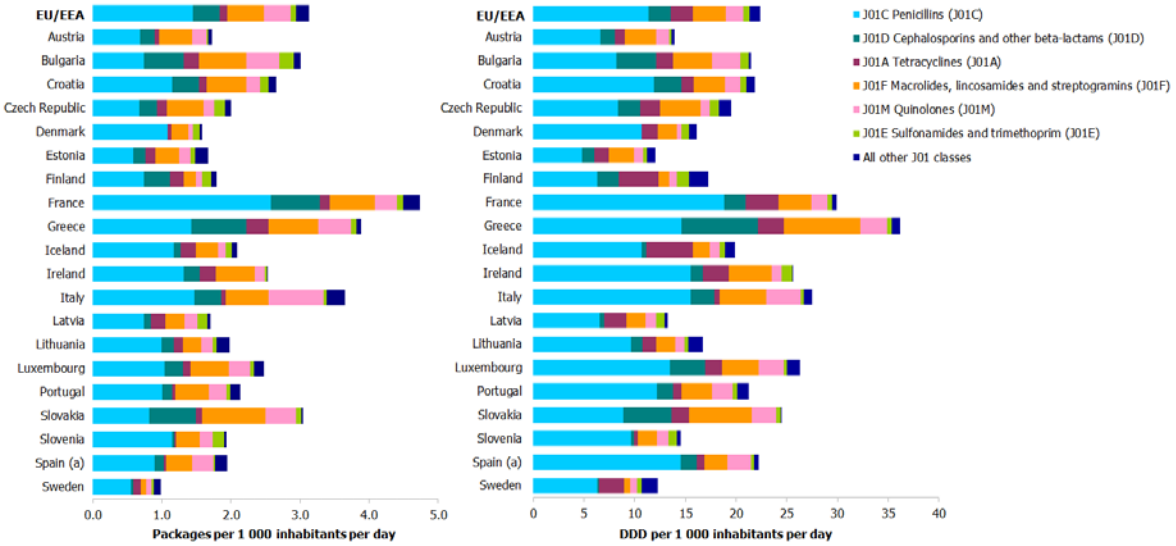
EU/EEA refers to the corresponding population-weighted mean consumption.

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

Indicator: packages per 1 000 inhabitants per day

In 2015, 20 countries reported data on the number of consumed packages of antibacterials for oral use in the community (i.e. outside hospitals) (Figure 3). On average, 3.1 packages of antibacterials for systemic use (ATC J01) were consumed per 1 000 inhabitants per day in EU/EEA countries in 2015. The total 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 4.7 in France (Table D8).

Figure 3. Consumption of antibacterials for systemic use (ATC group J01) and ATC group level 3 in the community, EU/EEA, 2015, expressed as packages per 1 000 inhabitants per day and DDD per 1 000 inhabitants per day



(a) Spain provided reimbursement data, i.e. not including consumption without a prescription and other non-reimbursed courses

EU/EEA refers to the corresponding population-weighted mean consumption based on 20 countries that provided data on packages.

The EU/EEA population-weighted mean consumption expressed as packages per 1 000 inhabitants per day did not show any statistically significant trend during the period 2011–2015 (Table D9). No country showed a statistically significant increasing trend. A statistically significant decreasing trend was observed for Denmark, Estonia, Finland, Luxembourg, Spain and Sweden.

Quality indicators for consumption of antibacterials for systemic use (ATC group J01) in the community

Relative consumption of beta-lactamase-sensitive penicillins, combination of penicillins including beta-lactamase inhibitors, third- and fourth-generation cephalosporins and fluoroquinolones and the ratio of broad- to narrow-spectrum antibacterials, the consensus-based ESAC quality indicators, are presented in Table D10 and Figures D1, D2, D3 and D4.

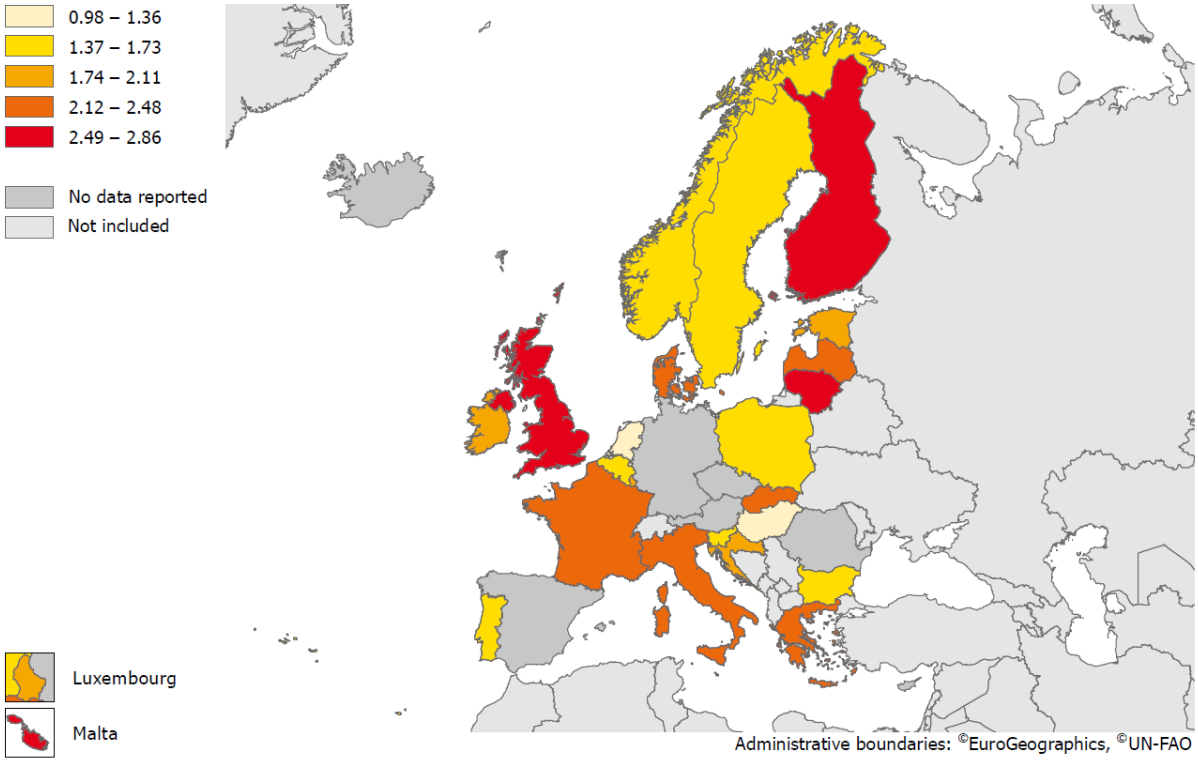
Consumption of antibacterials from other ATC groups (A07A, P01A, J04A)

Consumption of oral vancomycin (A07AA09), rifampicin (J04AB02) and oral and rectal metronidazole (P01AB01) are presented in Table D11.

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

In 2015, 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 1.0 in the Netherlands to 2.9 in Malta (Figure 4).

Figure 4. Consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, EU/EEA, 2015, 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 accordingly 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 2015 is presented in Table 3 and Figure 5. The proportions of cephalosporins, other beta-lactams (including carbapenems), and other groups of antibacterials were generally higher than in the community. However, substantial variation was observed across countries. For example, consumption of cephalosporins and other beta-lactams including carbapenems ranged from 7% in the United Kingdom to 55% in Bulgaria; consumption of macrolides, lincosamides and streptogramins from 4% in Sweden to 14% in Ireland, and consumption of quinolones from 4% in the United Kingdom to 19% in Malta and Italy.

Table 3. Consumption of antibacterials for systemic use (ATC group J01) in the hospital sector and antibacterial group, EU/EEA, 2015, expressed as DDD per 1 000 inhabitants per day

Country	Tetra-cyclines (J01A)	Beta-lactams, penicillins (J01C)	Other beta-lactam antibac-terials (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	0.01	0.85	0.36	0.03	0.09	0.18	0.12	0.02	1.67
Bulgaria	0.02	0.12	0.75	0.01	0.11	0.16	0.10	0.11	1.37
Croatia	0.04	0.59	0.58	0.04	0.15	0.24	0.17	0.10	1.90
Denmark	0.04	1.10	0.32	0.42	0.10	0.19	0.13	0.03	2.34
Estonia	0.06	0.54	0.58	0.05	0.16	0.18	0.14	0.04	1.74
Finland (a)	0.19	0.64	0.91	0.10	0.14	0.26	0.25	0.01	2.50
France	0.02	1.26	0.32	0.04	0.11	0.23	0.14	0.06	2.18
Greece	0.05	0.61	0.57	0.02	0.18	0.31	0.33	0.07	2.14
Hungary	0.04	0.37	0.34	0.03	0.13	0.22	0.07	0.03	1.23
Ireland	0.04	0.93	0.21	0.06	0.28	0.13	0.20	0.06	1.91
Italy	0.03	0.85	0.38	0.04	0.19	0.45	0.17	0.26	2.36
Latvia	0.11	0.63	0.68	0.08	0.17	0.33	0.18	0.07	2.24
Lithuania	0.07	1.05	0.74	0.06	0.06	0.28	0.20	0.09	2.54
Luxembourg	0.01	0.66	0.56	0.03	0.15	0.21	0.11	0.04	1.78
Malta	0.17	1.08	0.27	0.10	0.36	0.54	0.23	0.10	2.86
Netherlands	0.02	0.43	0.21	0.02	0.06	0.11	0.07	0.05	0.98
Norway	0.07	0.70	0.28	0.06	0.07	0.06	0.09	0.06	1.40
Poland	0.07	0.44	0.34	0.07	0.09	0.18	0.20	0.05	1.43
Portugal (b)	0.02	0.54	0.44	0.07	0.16	0.15	0.12	0.07	1.57
Slovakia	0.04	0.77	0.75	0.04	0.15	0.37	0.19	0.08	2.40
Slovenia	0.01	0.74	0.32	0.06	0.14	0.25	0.11	0.05	1.68
Sweden	0.20	0.91	0.18	0.06	0.07	0.16	0.08	0.01	1.67
United Kingdom	0.22	1.34	0.17	0.12	0.31	0.11	0.19	0.09	2.55
EU/EEA	**0.07**	**0.90**	**0.34**	**0.07**	**0.16**	**0.23**	**0.16**	**0.10**	**2.04**

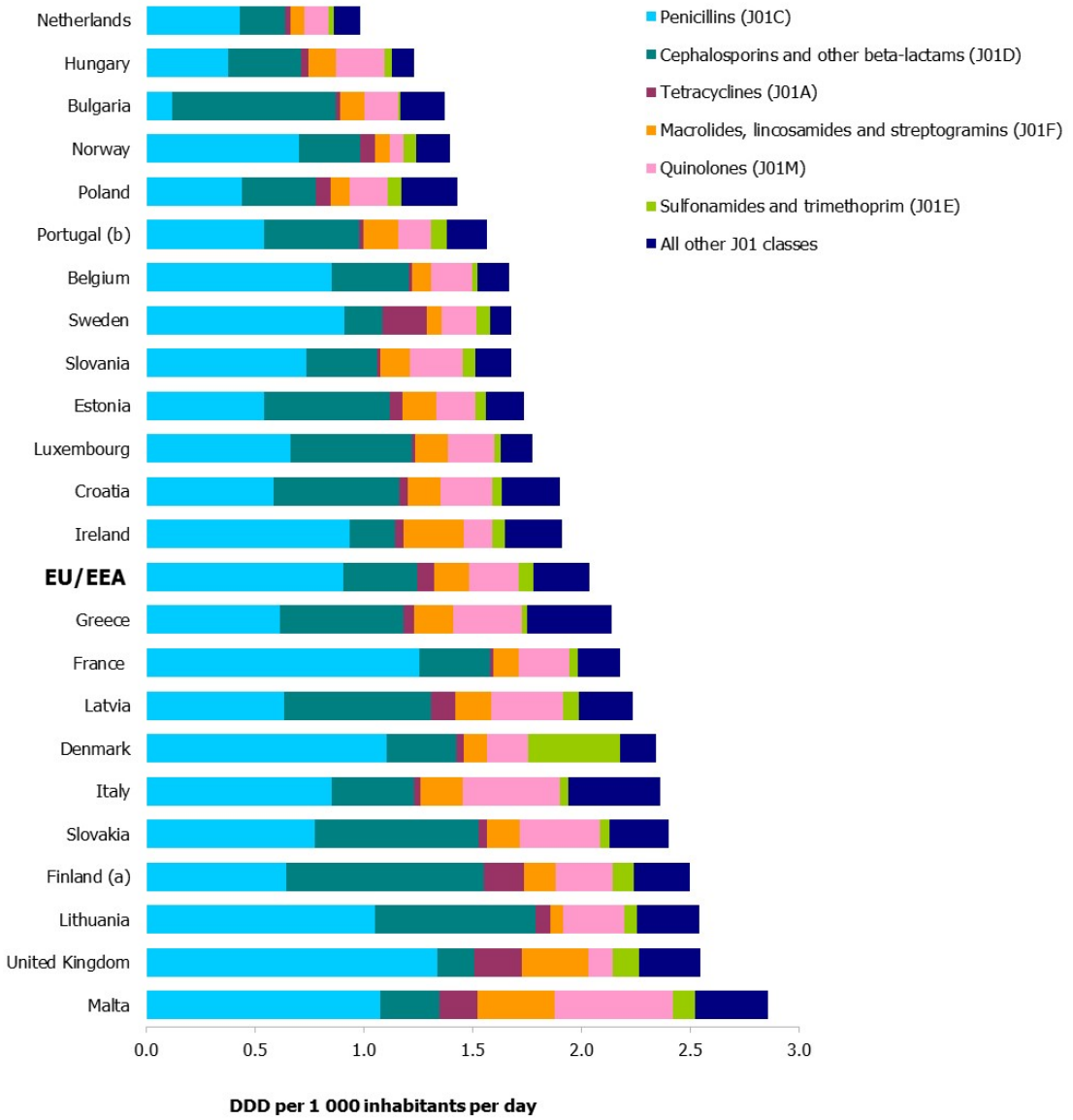
(a) Finland: data include consumption in remote primary healthcare centres and nursing homes.

(b) Portugal: data refer to public hospitals. Population was adjusted accordingly 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 5. Consumption of antibacterials for systemic use (ATC group J01) in the hospital sector and ATC group, EU/EEA, 2015, 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 accordingly based on hospital catchment area information provided by the country.

EU/EEA refers to the corresponding population-weighted mean consumption based on 23 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 2011–2015 (Table 4). A statistically significant increasing trend was observed for Denmark and Malta and a statistically significant decreasing trend for Finland and Luxembourg.

Table 4. Trends in consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, EU/EEA, 2011–2015, expressed as DDD per 1 000 inhabitants per day

Country	2011	2012	2013	2014	2015	Trends in antimicrobial consumption, 2011–2015	Average annual change 2011–2015	Statistically significant trend
Netherlands	0.97	0.96	0.95	0.95	0.98		0.00	
Hungary	1.20	1.23	1.20	1.25	1.23		0.01	
Bulgaria	1.41	1.37	1.38	1.40	1.37		0.00	
Norway	1.47	1.44	1.39	1.41	1.40		-0.02	
Poland				1.43	1.43		N/A	
Portugal (b)	1.45	1.46	1.64	1.55	1.57		0.03	
Belgium	2.02	1.71	1.67	1.60	1.67		-0.08	
Sweden	1.60	1.65	1.67	1.57	1.67		0.01	
Slovenia	1.66	1.56	1.55	1.61	1.68		0.01	
Estonia	1.75	2.00	1.79	1.81	1.74		-0.02	
Luxembourg	2.02	2.02	2.00	1.81	1.78		-0.07	↓
Croatia	1.88	1.97	1.79	1.85	1.90		-0.01	
Ireland	1.79	1.76	1.79	1.66	1.91		0.01	
EU/EEA	**1.93**	**1.95**	**2.03**	**2.00**	**2.04**		**0.03**	
Greece	2.00	1.90	2.00	2.11	2.14		0.05	
France	2.12	2.12	2.17	2.20	2.18		0.02	
Latvia	2.34	2.24	2.28	2.24	2.24		-0.02	
Denmark	1.74	1.78	2.02	2.13	2.34		0.16	↑
Italy	2.23	2.40	2.16	2.15	2.36		0.00	
Slovakia		2.02	2.30	2.47	2.40		N/A	
Finland (a)	3.09	2.79	2.77	2.64	2.50		-0.13	↓
Lithuania		2.39	2.39	2.35	2.54		N/A	
United Kingdom			2.45	2.59	2.55		N/A	
Malta	1.67	1.44	1.75	2.18	2.86		0.31	↑

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

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

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 2011 and 2015.

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

Carbapenems are antibacterial groups used for treating serious infections caused by multidrug-resistant gram-negative bacteria. Polymyxins - mainly colistin - have been used as last-resort antibacterials to treat infections caused by multidrug-resistant gram-negative bacteria that are resistant to carbapenems. Another group of antibacterials to treat infections caused by extended-spectrum-beta-lactamase (ESBL)-producing gram-negative bacteria are penicillins combined with beta-lactamase inhibitors (e.g. piperacillin/tazobactam).

In 2015, consumption of carbapenems was 0.05 DDD per 1 000 inhabitants per day (Table D12). Between 2011 and 2015, the EU/EEA population-weighted mean consumption of carbapenems did not show a statistically significant change (Table D12). A statistically significant increase was observed for five countries (Bulgaria, Croatia, Cyprus, Hungary and the Netherlands). None of the countries that reported data for all years during the period 2011–2015 showed a statistically significant decreasing trend.

The EU/EEA population-weighted mean consumption of polymyxins did not show any statistically significant change during the period 2011–2015 (Table D13). A statistically significant increase was observed for eight countries (Bulgaria, Denmark, Greece, Italy, Hungary, Malta, Norway and Romania). None of the countries reporting comparable data for all years during the period 2011–2015 showed a statistically significant decreasing trend.

The EU/EEA population-weighted mean consumption of piperacillin/tazobactam showed a statistically significant increasing trend for the period 2011–2015, as it did in most of the countries reporting hospital sector data.

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

In 2015, hospital consumption of oral vancomycin (ATC A07AA09) was reported from nine countries and ranged from 0.00003 DDD per 1 000 inhabitants per day in Italy to a maximum of 0.01 DDD per 1 000 inhabitants per day in Denmark.

Oral and rectal nitroimidazole consumption in hospitals was reported by 20 countries ranging from 0.004 DDD per 1 000 inhabitants per day in Lithuania to 0.06 DDD per 1 000 inhabitants per day in the UK. Metronidazole represented almost 100% of all nitroimidazole derivatives in the reporting countries.

Rifampicin (ATC J04AB02) consumption in 2015, reported in 19 countries, ranged from a minimum of 0.005 DDD per 1 000 inhabitants per day in Greece to a maximum of 0.15 DDD per 1 000 inhabitants per day in Lithuania.

Consumption of oral vancomycin (A07AA09), rifampicin (J04AB02) and oral and rectal metronidazole (P01AB01) are presented in the Table D14.

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

In 2015, 28 countries reported data on consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01B) in the community (Table D15 and Figure D5).

The EU/EEA population-weighted mean consumption was 0.96 DDD per 1 000 inhabitants per day. The consumption varied by a factor of nine, ranging from 0.34 (Croatia) to 3.1 DDD per 1 000 inhabitants per day (Belgium).

In 2015, terbinafine (D01B02), fluconazole (J02AC01), and itraconazole (J02AC02) made up 90% of the total consumption of antimycotics and antifungals for systemic use in the community in all countries except Slovakia.

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

In 2015, 21 countries reported data on consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01B) in the hospital sector (Table D16, Figure D6).

The EU/EEA population-weighted mean consumption was 0.084 DDD per 1 000 inhabitants per day. Consumption varied by a factor of five from 0.033 DDD per 1 000 inhabitants per day (Bulgaria) to 0.188 (Denmark).

In 2015, fluconazole (J02AC01) accounted for 66% of the total consumption of antimycotics and antifungals for systemic use in the hospital sector in the reporting countries. Fluconazole consumption, as a proportion of the total, varied from 42% (Malta) to 96% (Bulgaria).

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

Twenty-eight countries reported data on antivirals for systemic use (ATC group J05) in 2015. The data are pooled across the two sectors (Table D17 and Figure D7). Austria, the Czech Republic, Germany, Iceland, the Netherlands and Spain only reported 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 for both sectors was 2.7 DDD per 1 000 inhabitants per day. Country-specific consumption showed a 10-fold difference from 0.59 DDD per 1 000 inhabitants per day (Croatia) to 5.5 (Portugal).

The EU/EEA population-weighted mean consumption in the reporting countries was the highest for combinations of antivirals for treatment of HIV infections (ATC group J05AR) (0.84 DDD per 1 000 inhabitants per day).

Table D18 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 58% of the total consumption of antivirals for systemic use (ATC group J05) in the reporting countries. The relative consumption of HIV/AIDS antivirals of the total antiviral consumption ranged from 0.4% (Poland) to 91% (Estonia).

Malta reported the highest proportion of consumption of HIV/hepatitis B antivirals (32%) and Romania of hepatitis B antivirals (21%).

The proportion of the consumption of hepatitis C antivirals out of the total consumption of antivirals for systemic use (ATC group J05) ranged from 0.7% (Poland) to 11% (Czech Republic). In 2015, direct acting antivirals (DAA) were under surveillance within this group and half of the countries reported consumption.

For herpes antivirals, the proportion of the total of antivirals for systemic use (ATC group J05) consumed ranged from 0.0007% (Italy) to 100% (Spain).

In 2015, the EU/EEA population-weighted mean consumption of substances used for the treatment of influenza (rimantadine; ATC code J05AC02, zanamivir; ATC code J05AH01 and oseltamivir; ATC code J05AH02) was 0.03 DDD per 1 000 inhabitants per day. Consumption ranged from <0.001 DDD per 1 000 inhabitants per day in Luxembourg, where it accounted for 0.012% of the total antivirals for systemic use (ATC J05) consumed, to 0.29 DDD per 1 000 inhabitants per day in Lithuania, accounting for 14% of the total consumption of antivirals for systemic use. Lithuania reported the highest proportion of consumption of anti-influenza substances (25%).

Discussion

European countries are increasingly taking action to control antimicrobial resistance through the rational use of antimicrobials, including awareness campaigns on their prudent use. Data reported by EU/EEA countries to ESAC-Net are instrumental for the evaluation of such action both at national and international level.

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 this does not include antimicrobials dispensed without a prescription and non-reimbursed prescribed antimicrobials [8]. 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 as such in the tables and figures of this report. In addition, type (source) of data in individual countries may change from one year to another, possibly affecting the results of pattern and trends in antimicrobial drug consumption. For this report the type of data provided by the countries was the same as in the previous report (2013–2014) with the exception of one country.

Broadly accepted standards and metrics reflecting responsible antibiotic use have not been defined until now. The development of evidence-based and consensually validated quantity metrics to evaluate antibiotic use, both for community and hospital settings, was one of the objectives of 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). The project has proposed quality indicators and quantity metrics for antibiotics use[1]. The proposed metrics have been used in this report.

Inappropriate antibacterial consumption in hospitals accelerates the emergence and spread of multidrug-resistant bacteria responsible for healthcare-associated infections and is now becoming a global healthcare issue [9,10].

In 2015, consumption of antibacterials for systemic use (ATC group J01) in the community in Europe varied considerably between countries with a north-to-south gradient. There are many reasons for these large differences, some of which are cultural determinants [11]. This report shows that the EU/EEA population-weighted mean consumption of antibacterials for systemic use (ATC group J01) in the community did not undergo any statistically significant change during the period 2011–2015. No country showed a statistically significant increasing trend for the period 2011–2015, but statistically significant decreasing trends were observed for Finland, the Netherlands and Sweden.

The differences in the ranking positions of some countries compared with their ranking when reporting 'DDD per 1 000 per inhabitants per day' probably reflect differences in the number of items or the dose per item in antibiotic packages. For countries dispensing complete packages for community prescriptions, consumption data expressed in 'packages per 1 000 inhabitants per day' may be a surrogate measure for the prescribing frequency (i.e. number of prescriptions). It can be used for the assessment of national trends in antibacterial prescribing and the impact of antimicrobial awareness campaigns where prescription data are not available. The decrease in the number of packages in some countries probably reflects a reduction in antibacterial prescriptions between 2011 and 2015, although this should be confirmed with national data from other sources.

Since patients are not treated with antibiotics continuously every day of the year, a more understandable way to illustrate the meaning of the indicator DDD per 1 000 inhabitants per day may be the 'number of DDD (or packages) per person (inhabitant) per year'.

An estimate of the number of days for which, on average, each person is treated with an antibiotic annually 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

[1] http://drive-ab.eu/wp-content/uploads/2014/09/WP1A_Final-QMs-QIs_final.pdf

EU/EEA in 2015 it was 8.2 DDD per person per year. In other words, in 2015 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 (ATC group J01F) will probably result in an increase in the ratio of broad- to narrow-spectrum penicillins, cephalosporins and macrolides. For countries where changes in the ranking suggest quality improvement, this may just reflect a relative change compared to other countries. In other words, quality decreased in all countries but less so in the specific country in question [12]. It should be emphasised that these indicators cannot by themselves denote quality of antimicrobial use unless they are used with corresponding clinical data (e.g. resistance pattern).

Indications for antimicrobial prescriptions and detailed information on current national programmes would be required to identify the factors and reasons behind annual changes in antimicrobial consumption in EU/EEA countries.

The types of healthcare facilities included in the hospital sector differ across European 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. In Malta the true national consumption of antimicrobials in both sectors could be affected by the number of tourists and this may contribute to the total antimicrobial consumption. 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 antimicrobial subclasses in the hospital sector for all countries. The proportions of cephalosporins, other beta-lactams (including carbapenems) and other groups of antimicrobials were generally higher than in the community.

The prevalence of antibiotic-resistant microorganisms, including multi drug-resistant (MDR) strains is increasing, especially in hospitals where selective antibiotic pressure is present. Treating infections caused by these bacteria became a serious threat, as there are fewer or sometimes no effective antimicrobial agent available.

Patients receiving antimicrobials are more likely to become colonised with resistant bacteria and therefore are at greater risk of developing subsequent infections with these bacteria than patients who do not receive antimicrobials. Resistant microorganisms are transmitted from patient to patient and are further selected following antibiotic exposure. The spread of resistant bacteria in healthcare facilities has become a public health threat. One significant driver for the selection of highly-resistant bacteria responsible for healthcare-associated infections in hospitalised patients is the use of specific, broad spectrum and mostly reserve or last-line antimicrobials in hospitals.

Carbapenems are the last-line group of antimicrobials and are mainly used in hospitals to treat patients with confirmed or suspected infections involving MDR microorganisms. Use of a carbapenems is a risk factor for subsequent infection with a 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 antibacterial groups such as polymyxins are available for the treatment of patients infected with such bacteria [9,13].

Assuming that the average duration of carbapenem treatment is 10 days, the consumption of 0.05 DDD per 1 000 inhabitants per day corresponds to more than one million carbapenem treatment courses administered in the EU/EEA each year.

The latest data from the European Antimicrobial Resistance Surveillance Network (EARS-Net) show a statistically significant increase in the population-weighted EU/EEA mean percentage of carbapenem resistance in K*lebsiella pneumoniae* isolates from invasive infections. This poses a great concern and a threat to patient safety in Europe.

The second Joint Interagency Antimicrobial Consumption and Resistance Analysis (JIACRA) report from ECDC, the European Food Safety Authority (EFSA) and the European Medicines Agency (EMA) showed a strong association between carbapenem consumption and the percentage of carbapenem-resistant invasive *Klebsiella pneumoniae* isolates in EU/EEA countries reporting these data [14].

Carbapenem-resistant bacteria are highly drug-resistant and only a few antimicrobial groups such as polymyxins (e.g. colistin) are available for treating patients infected with such bacteria.

The consumption pattern in antimycotics and antifungals for systemic use in the hospital sector was different from the community pattern. In the hospital sector, 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 between countries. Increasing numbers 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 analysis may highlight certain socioeconomic or structural determinants that would explain this variation.

Public health conclusions

Antimicrobial resistance is a serious threat to public health and antimicrobial use is one of the main drivers of resistance. Global efforts to control the emergence of resistance include continuous monitoring of antimicrobial drug use. As resistance patterns and trends differ across countries, the extent, pattern and trends of antimicrobial drug consumption also differ. Thus, to understand antimicrobial resistance epidemiology in Europe requires reliable national antimicrobial consumption data.

Excessive antibiotic use in hospitals accelerates the emergence and spread of multidrug-resistant bacteria responsible for healthcare-associated infections. The fact that consumption of some last-line groups of antimicrobials has increased in the hospital sector in some European countries is a concern. It may indicate that MDR spread has reached a level where other antibacterials have become ineffective.

Inappropriate antibiotic prescribing may contribute to a critical situation where there are no effective treatment options available for patients with bacterial infections.

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

References

1. European Centre for Disease Prevention and Control. Introduction to the Annual epidemiological report for 2016. In: ECDC. Annual epidemiological report for 2016. Stockholm: ECDC; 2018. Available from: https://ecdc.europa.eu/en/annual-epidemiological-reports-2016/methods.
2. European Centre for Disease Prevention and Control. Surveillance systems overview [internet, downloadable spreadsheet]. Stockholm: ECDC; 2018. Available from: https://ecdc.europa.eu/en/publications-data/surveillance-systems-overview-2016
3. European Centre for Disease Prevention and Control. Surveillance atlas of infectious diseases [internet]. Stockholm: ECDC; 2017 [cited 30 Jan 2018]. Available from: http://atlas.ecdc.europa.eu/public/index.aspx
4. WHO Collaborating Centre for Drug Statistics Methodology. ATC Index with DDDs. Oslo, WHO 2018 Available from: https://www.whocc.no/atc_ddd_index/
5. 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
6. European Centre for Disease Prevention and Control. Antimicrobial consumption surveillance in Europe 2012. Annual report of the European Antimicrobial Consumption Surveillance Network (ESAC-Net). Stockholm: ECDC; 2014. Available from http://ecdc.europa.eu/en/publications/Publications/antimicrobial-consumption-europe-esac-net-2012.pdf
7. European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2016. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Stockholm: ECDC; 2017. Available from https://ecdc.europa.eu/sites/portal/files/documents/AMR%202016_Final-with-cover-for-web-2017.pdf
8. Safrany N, Monnet DL. Antibiotics obtained without a prescription in Europe. Lancet Infect Dis. 2012 Mar;12(3):182-3
9. 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. 2017;6:113.
10. European Centre for Disease Prevention and Control. Proposals for EU guidelines on the prudent use of antimicrobials in humans. Stockholm: ECDC; 2017 https://ec.europa.eu/health/amr/sites/amr/files/amr_guidelines_prudent_use_en.pdf
11. Borg MA. Cultural determinants of infection control behaviour: understanding drivers and implementing effective change. J Hosp Infect. 2014 Mar;86(3):161-8.
12. 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
13. EUROROUNDUPS. Carbapenemase-producing *Enterobacteriaceae* in Europe: assessment by national experts from 38 countries. Euro Surveill. 2015;20(45):pii=30062.
14. ECDC (European Centre for Disease Prevention and Control), EFSA (European Food Safety Authority), and EMA (European Medicines Agency), 2017. 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 2017;15(7):4872, 135 pp. doi:10.2903/j.efsa. 2017.4872. Available from https://ecdc.europa.eu/sites/portal/files/documents/efs2_4872_final.pdf