SURVEILLANCE REPORT

Annual Epidemiological Report for 2016

Antimicrobial consumption

Key facts

- Twenty-nine countries, including 27 EU Member States and two EEA countries (Iceland and Norway) reported data on antimicrobial consumption for the community, i.e. outside hospitals, and 23 countries reported data for the hospital sector in 2016.
- In the community, the average consumption of antibacterials for systemic use (Anatomical Therapeutic Chemical (ATC) group J01) was 21.9 DDD per 1 000 inhabitants per day (country range: 10.4-36.3) in 2016. During the period 2012–2016, no statistically significant change was observed for the EU/EEA overall. However, a statistically significant increasing trend was observed for Greece and Spain, and a statistically significant decreasing trend was observed for Finland, Luxembourg, Norway and Sweden.
- The average consumption of antimycotics and antifungals for systemic use (ATC groups J02 and D01B) in the community was 1.0 DDD per 1 000 inhabitants per day (country range: 0.37–3.1).
- In the hospital sector, the average consumption of antibacterials for systemic use was 2.1 DDD per 1 000 inhabitants per day (country range: 1.0-2.9). During the period 2012–2016, no statistically significant change was observed for the EU/EEA overall. However, statistically significant increasing trends were observed for Greece, Malta and Slovenia, and statistically significant decreasing trends were observed for Estonia, Finland and Luxembourg.
- The average consumption of carbapenems was 0.05 DDD per 1 000 inhabitants per day (country range: 0.03–0.18) and this did not change significantly between 2012 and 2016. However, a statistically significant increasing trend was observed for ten countries and one country showed a statistically significant decreasing trend during the same period.
- The average consumption of polymyxins was 0.015 DDD per 1 000 inhabitants per day (country range: <0.001–0.102) and did not show any statistically significant change during the period 2012–2016. A statistically significant increasing trend was observed for nine countries but also a statistically significant decreasing trend in two countries.
- The average consumption of antimycotics and antifungals for systemic use (ATC groups J02 and D01B) was 0.06 DDD per 1 000 inhabitants per day (country range: 0.02-0.18).
- The average consumption of antivirals for systemic use (ATC group J05) in both sectors (community and hospital sector) in 2016 was 3.0 DDD per 1 000 inhabitants per day (country range: 0.21–7.4).

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Stockholm, June 2018

Methods

This report is based on data for 2016 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 data for 2016 collected at European level. Twenty-seven EU Member States and two EEA countries (Iceland and Norway) reported 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 2017 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 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 not available, 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.

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, presenting data with the same denominator enables cross-sectorial comparison.

For the countries which provided data on the number of packages of antibacterials for oral use consumed in the community, this report uses an additional indicator - 'packages per 1 000 inhabitants per day'. This indicator may be used at national level 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

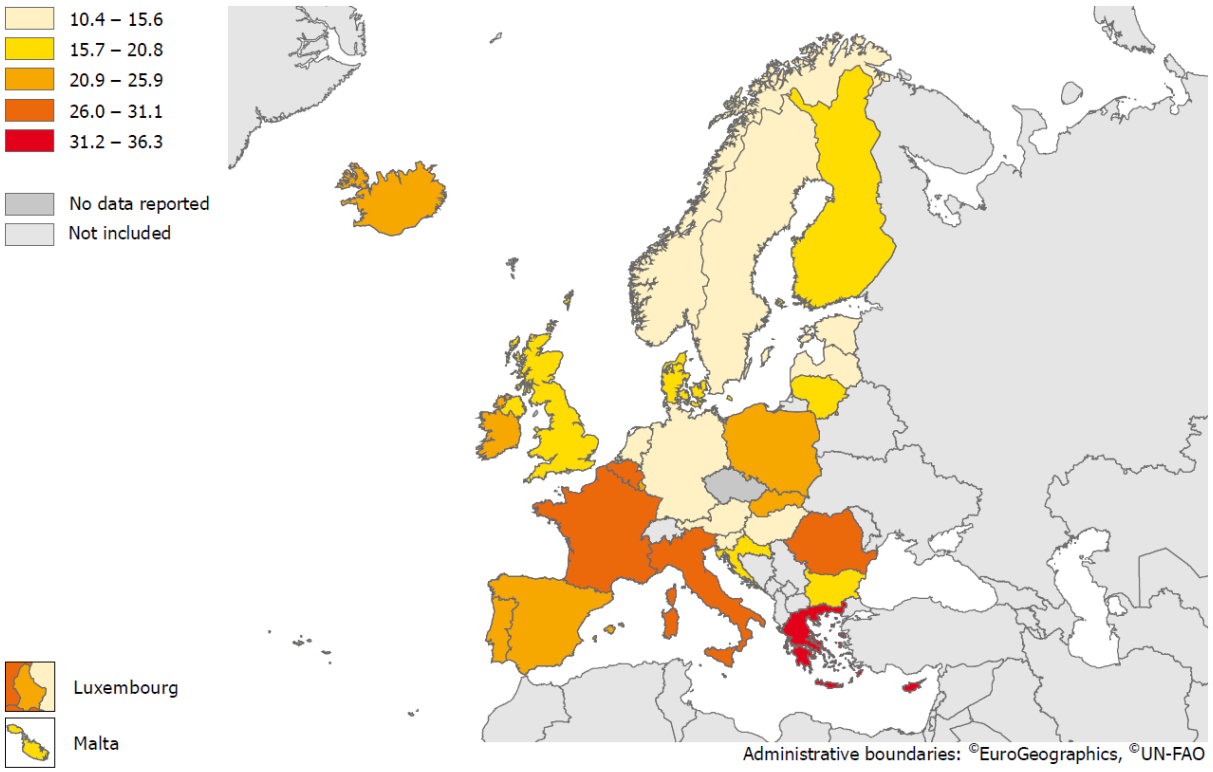
All EU Member States, except the Czech Republic, and two EEA countries (Iceland and Norway) reported antimicrobial consumption for the community sector and 23 countries reported for the hospital sector in 2016. Two countries (Cyprus and Romania) reported data on total consumption in the country – i.e. 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.

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

Indicator: DDD per 1 000 inhabitants per day

In 2016, the EU/EEA population-weighted mean consumption of antibacterials for systemic use in the community (i.e. outside hospitals) was 21.9 DDD per 1 000 inhabitants per day, ranging from 10.4 in the Netherlands to 36.3 in Greece **(**Figure 1).

Figure 1. Consumption of antibacterials for systemic use (ATC group J01) in the community, EU/EEA countries, 2016, 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 2016 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 33% (Germany) to 67% (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 23% (Slovakia); and quinolone antibacterials (ATC group J01M), from 2% (United Kingdom) to 21% (Cyprus).

Table 1. Consumption of antibacterials for systemic use (ATC group J01) and ATC group level 3 in the community, EU/EEA countries, 2016, expressed as DDD per 1 000 inhabitants per day

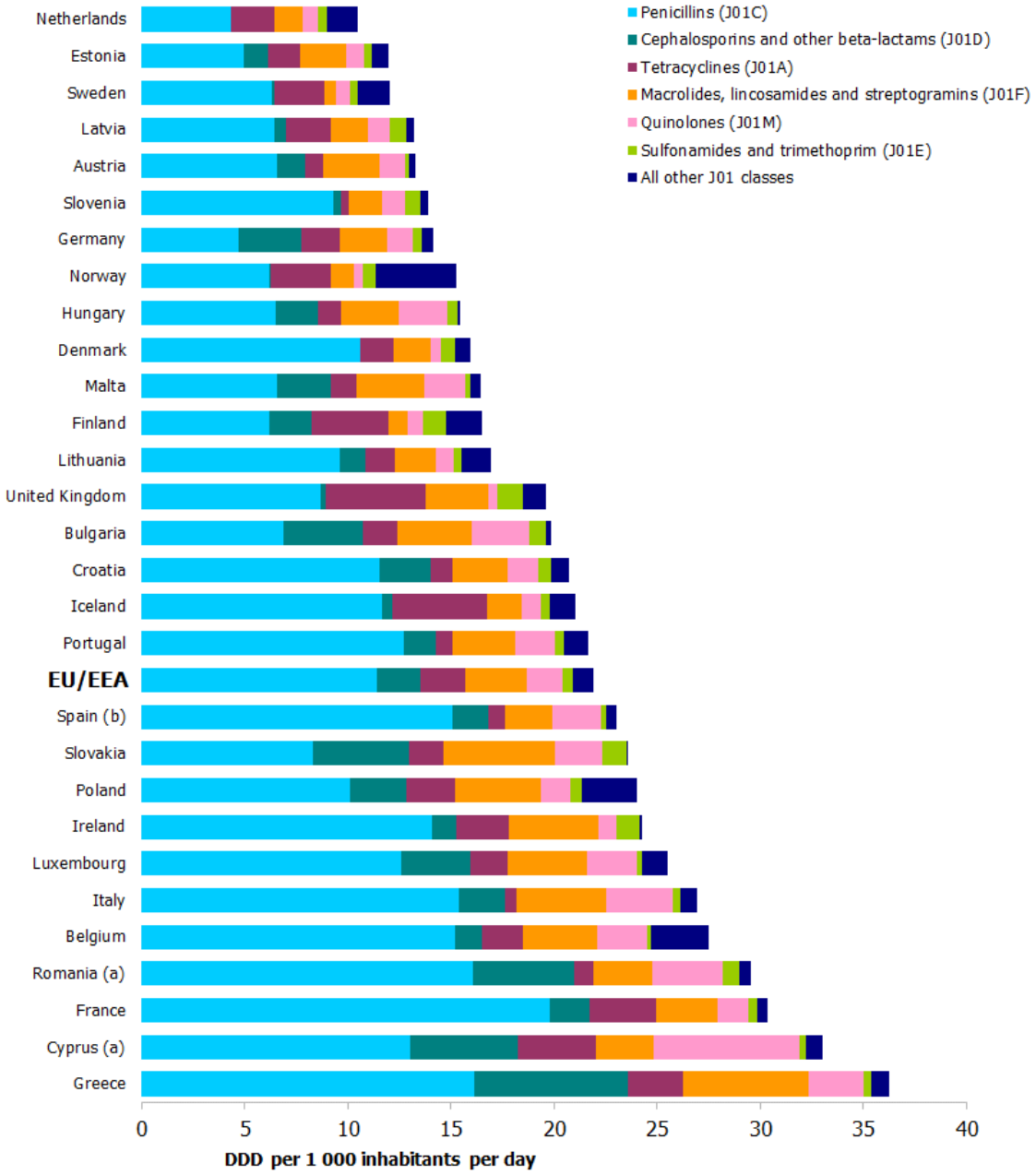
Country	Tetra-cyclines (J01A)	Beta-lactams, penicillins (J01C)	Other beta-lactam antibac-terials (J01D)	Sulfon-amides and trimetho-prim (J01E)	Macrolides, lincosamides and strepto-gramins (J01F)	Quino-lones (J01M)	Other antibac-terials (J01X)	Sum (J01B, J01G, and J01R)*	Total (ATC group J01)
Austria	0.9	6.5	1.4	0.2	2.7	1.2	0.3	0.0	13.3
Belgium	2.0	15.2	1.3	0.2	3.6	2.4	2.8	0.0	27.5
Bulgaria	1.7	6.9	3.8	0.8	3.6	2.8	0.1	0.2	19.8
Croatia	1.0	11.5	2.5	0.6	2.7	1.5	0.9	0.0	20.7
Cyprus (a)	3.8	13.0	5.2	0.3	2.8	7.1	0.7	0.1	33.0
Denmark	1.6	10.6	0.0	0.7	1.8	0.5	0.7	0.0	15.9
Estonia	1.6	4.9	1.2	0.4	2.3	0.8	0.8	0.0	12.0
Finland	3.7	6.2	2.1	1.1	0.9	0.7	1.7	0.0	16.5
France	3.2	19.8	1.9	0.4	3.0	1.5	0.5	0.0	30.3
Germany	1.9	4.7	3.0	0.5	2.3	1.2	0.5	0.0	14.1
Greece	2.7	16.1	7.5	0.4	6.1	2.6	0.8	0.1	36.3
Hungary	1.1	6.5	2.1	0.5	2.8	2.4	0.1	0.0	15.4
Iceland	4.6	11.6	0.5	0.5	1.7	0.9	1.2	0.0	21.0
Ireland	2.5	14.1	1.2	1.1	4.4	0.9	0.1	0.0	24.2
Italy	0.6	15.4	2.3	0.4	4.3	3.2	0.7	0.1	26.9
Latvia	2.2	6.4	0.6	0.8	1.8	1.0	0.3	0.0	13.2
Lithuania	1.5	9.6	1.2	0.3	2.0	0.9	1.4	0.0	16.9
Luxembourg	1.8	12.6	3.4	0.3	3.8	2.4	1.2	0.0	25.5
Malta	1.2	6.5	2.6	0.3	3.3	2.0	0.2	0.3	16.4
Netherlands	2.1	4.3	0.0	0.4	1.4	0.7	1.5	0.0	10.4
Norway	2.9	6.2	0.1	0.7	1.1	0.4	3.9	0.0	15.2
Poland	2.3	10.1	2.8	0.6	4.2	1.4	2.6	0.0	24.0
Portugal	0.8	12.7	1.5	0.4	3.1	1.9	1.1	0.0	21.6
Romania (a)	0.9	16.0	5.0	0.8	2.8	3.4	0.3	0.3	29.5
Slovakia	1.7	8.3	4.6	1.2	5.4	2.3	0.1	0.0	23.6
Slovenia	0.4	9.3	0.3	0.7	1.6	1.1	0.4	0.0	13.9
Spain (b)	0.8	15.1	1.7	0.2	2.3	2.4	0.5	0.0	23.0
Sweden	2.4	6.3	0.1	0.4	0.5	0.7	1.6	0.0	12.0
United Kingdom	4.9	8.7	0.3	1.2	3.0	0.4	1.1	0.0	19.6
EU/EEA	**2.2**	**11.4**	**2.1**	**0.6**	**3.0**	**1.7**	**0.9**	**0.0**	**21.9**

(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 countries, 2016, 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 of antibacterials for systemic use decreased from 22.4 DDD per 1 000 inhabitants per day in 2015 to 21.9 in 2016, but there was no statistically significant trend for the five-year period 2012–2016 (Table 2). Greece and Spain showed a statistically significant increasing trend for this period. A statistically significant decreasing trend was observed for Finland, Luxembourg, Norway and Sweden.

Table 2. Trends in consumption of antibacterials for systemic use (ATC group J01) in the community, EU/EEA countries, 2012–2016, expressed as DDD per 1 000 inhabitants per day

Country	2012	2013	2014	2015	2016	Trends in antimicrobial consumption, 2012–2016	Average annual change 2012–2016	Statistically significant trend
Netherlands	11.3	10.8	10.6	10.7	10.4		-0.19	
Estonia	11.7	11.7	11.7	12.0	12.0		0.07	
Sweden	14.1	13.0	13.0	12.3	12.0		-0.48	↓
Latvia	13.0	13.5	12.6	13.3	13.2		0.01	
Austria	14.0	16.3	13.9	14.0	13.3		-0.37	
Slovenia	14.3	14.5	14.2	14.5	13.9		-0.08	
Germany	14.8	15.7	14.6	14.3	14.1		-0.27	
Norway	16.9	16.2	15.9	15.8	15.2		-0.38	↓
Hungary	15.0	15.5	16.2	17.0	15.4		0.23	
Denmark	16.4	16.4	15.9	16.1	15.9		-0.13	
Malta	22.5	23.8	23.7	22.2	16.4		-1.37	
Finland	19.5	18.3	18.1	17.2	16.5		-0.71	↓
Lithuania	16.2	18.5	16.0	16.7	16.9		-0.03	
United Kingdom	20.1	20.6	20.8	20.1	19.6		-0.15	
Bulgaria	18.5	19.9	21.2	21.4	19.8		0.42	
Croatia	21.7	21.1	21.4	21.8	20.7		-0.12	
Iceland	22.1*	21.9*	19.3	19.9	21.0		N/A	
Portugal	22.7	19.6†	20.3†	21.3†	21.6†		N/A	
EU/EEA	**21.7**	**22.3**	**21.9**	**22.4**	**21.9**		**0.05**	
Spain	19.7†	20.3†	21.6†	22.2†	23.0†		0.86	↑
Slovakia	20.0	23.6	20.9	24.5	23.6		0.80	
Poland	22.9	23.6	22.8	26.2	24.0		0.47	
Ireland	23.0	23.8	23.1	25.6	24.2		0.42	
Luxembourg	27.7	27.7	25.8	26.3	25.5		-0.57	↓
Italy	27.5	28.6	27.8	27.5	26.9		-0.24	
Belgium	29.8	29.6	28.5	29.3	27.5		-0.48	
Romania	30.4*	31.6*	31.2*	33.3*	29.5*		0.00	
France	29.7	30.1	29.0	29.9	30.3		0.11	
Cyprus	29.7*	28.2*	26.1*	31.1*	33.0*		0.95	
Greece	32.5	32.2	35.1	36.1	36.3		1.15	↑
Czech Republic	17.5	18.9	19.1	19.5			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 2012 and 2016.

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

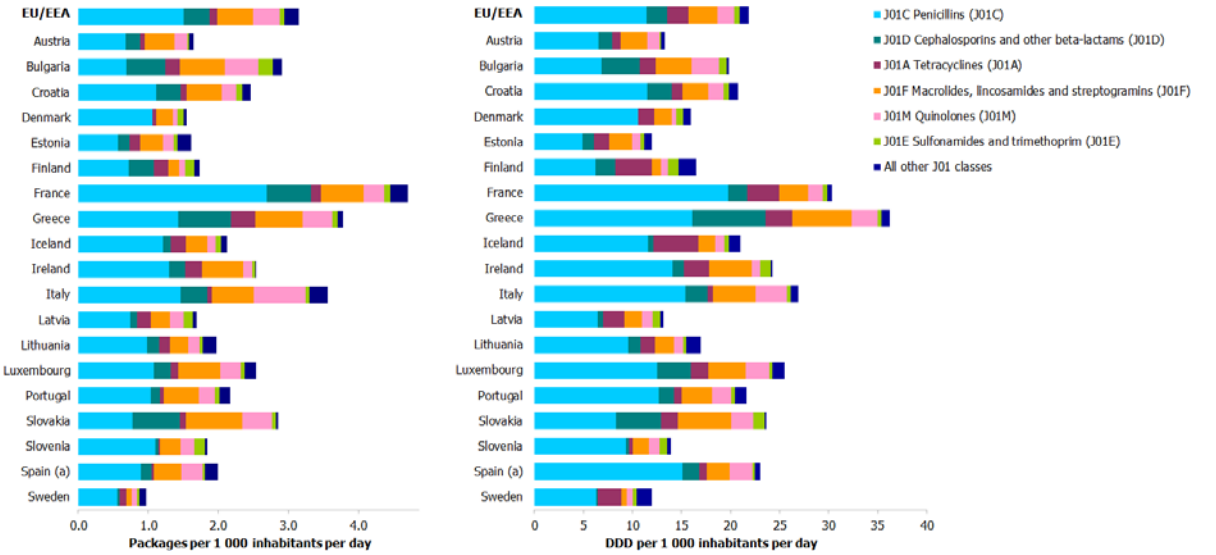
EU/EEA refers to the corresponding population-weighted mean consumption.

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 2016, 19 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 2016. 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 countries, 2016, 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 19 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 2012–2016 (Table D9). No country showed a statistically significant increasing trend. A statistically significant decreasing trend was observed for Denmark, Estonia, Finland 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 - i.e. the consensus-based ESAC quality indicators, are presented in Table D10 and Figures D1, D2, D3 and D4.

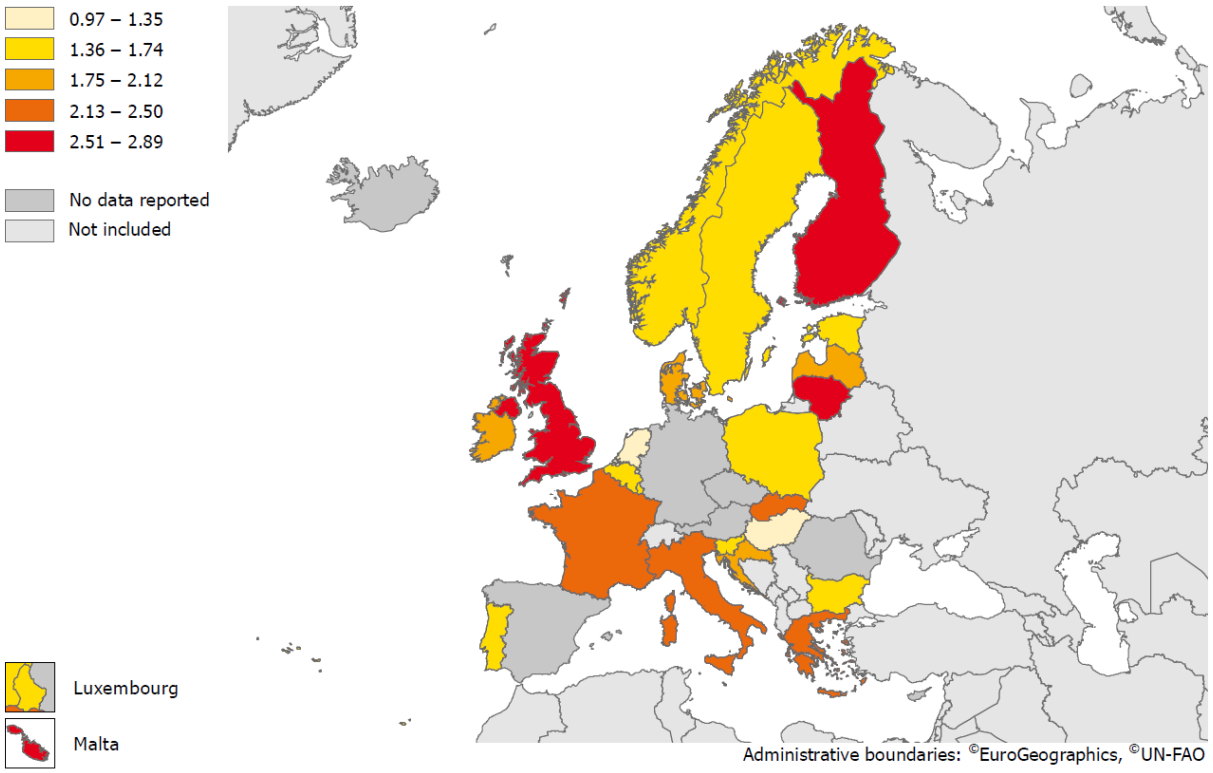
Consumption of antibacterials from other ATC groups (A07A, P01A, J04A)

Ten countries reported community consumption of oral vancomycin (A07AA09), while consumption of rifampicin (J04AB02) and oral and rectal metronidazole (P01AB01) were reported by 27 and 29 countries, respectively (Table D11).

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

In 2016, the EU/EEA population-weighted mean consumption of antibacterials for systemic use in the hospital sector was 2.1 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 countries, 2016, 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 2016 is presented in Table 3 and Figure 5. However, 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 61% in Bulgaria; consumption of macrolides, lincosamides and streptogramins (ATC group J01F) from 3% in Lithuania to 15% in Ireland, and consumption of quinolones (ATC group J01M) from 4% in the Norway to 18% in Hungary.

Table 3. Consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, by ATC group, EU/EEA countries, 2016, 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	0.83	0.34	0.03	0.09	0.18	0.12	0.02	1.63
Bulgaria	0.02	0.12	0.98	0.01	0.11	0.17	0.12	0.11	1.63
Croatia	0.04	0.59	0.54	0.04	0.15	0.25	0.18	0.09	1.87
Denmark	0.04	1.10	0.29	0.11	0.11	0.16	0.14	0.04	1.99
Estonia	0.04	0.57	0.57	0.05	0.13	0.16	0.15	0.03	1.70
Finland (a)	0.18	0.66	0.99	0.09	0.13	0.25	0.21	0.01	2.52
France	0.02	1.27	0.34	0.04	0.11	0.24	0.13	0.05	2.19
Greece	0.06	0.86	0.58	0.02	0.15	0.26	0.37	0.08	2.39
Hungary	0.03	0.37	0.33	0.03	0.11	0.22	0.07	0.03	1.18
Ireland	0.04	0.91	0.20	0.05	0.26	0.11	0.19	0.07	1.83
Italy	0.03	0.84	0.32	0.05	0.18	0.42	0.18	0.46	2.47
Latvia	0.10	0.57	0.64	0.08	0.13	0.32	0.19	0.06	2.10
Lithuania	0.06	1.08	0.76	0.06	0.07	0.27	0.23	0.07	2.59
Luxembourg	0.01	0.60	0.56	0.03	0.14	0.23	0.12	0.04	1.73
Malta	0.32	1.28	0.26	0.07	0.33	0.35	0.19	0.09	2.89
Netherlands	0.02	0.43	0.21	0.03	0.06	0.11	0.07	0.04	0.97
Norway	0.07	0.70	0.27	0.06	0.07	0.06	0.09	0.06	1.38
Poland	0.00	0.40	0.45	0.06	0.07	0.24	0.12	0.02	1.36
Portugal (b)	0.02	0.56	0.44	0.07	0.17	0.14	0.12	0.06	1.58
Slovakia	0.04	0.86	0.77	0.05	0.14	0.36	0.20	0.07	2.49
Slovenia	0.02	0.75	0.32	0.06	0.13	0.24	0.12	0.06	1.69
Sweden	0.18	0.90	0.18	0.06	0.06	0.16	0.08	0.02	1.65
United Kingdom	0.23	1.37	0.17	0.12	0.29	0.12	0.20	0.09	2.58
EU/EEA	**0.07**	**0.92**	**0.35**	**0.06**	**0.15**	**0.23**	**0.15**	**0.13**	**2.06**

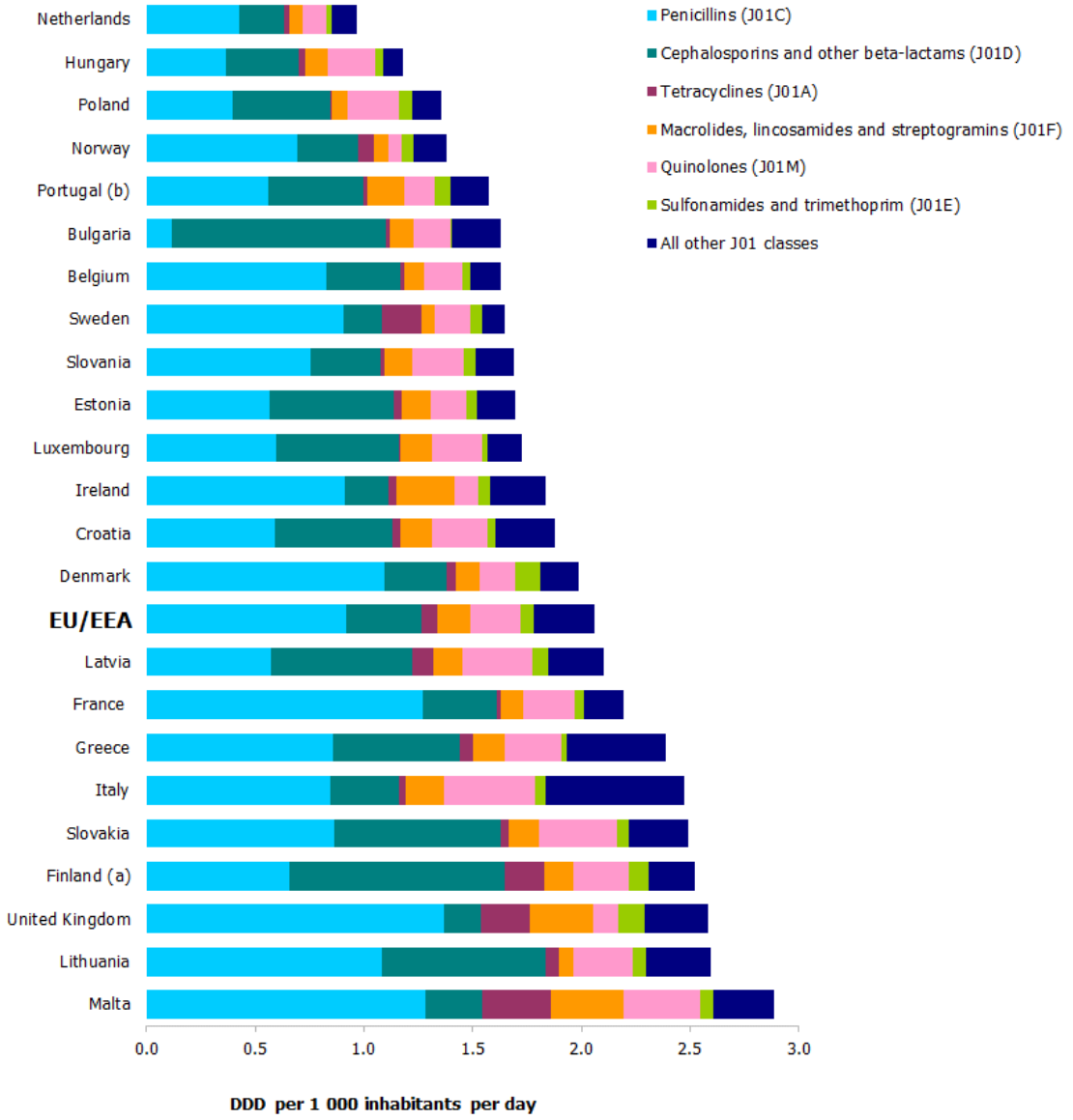
(a) Finland: data include consumption in remote primary healthcare centres and nursing homes.

(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 5. Consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, by ATC group, EU/EEA countries, 2016, 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 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 2012–2016 (Table 4). Statistically significant increasing trends were observed for Greece, Malta and Slovenia, and statistically significant decreasing trends were observed for Estonia, Finland and Luxembourg.

Table 4. Trends in consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, EU/EEA countries, 2012–2016, expressed as DDD per 1 000 inhabitants per day

Country	2012	2013	2014	2015	2016	Trends in antimicrobial consumption, 2012-2016	Average annual change 2012-2016	Statistically significant trend
Netherlands	0.96	0.95	0.95	0.98	0.97		0.00	
Hungary	1.23	1.20	1.25	1.23	1.18		-0.01	
Poland			1.43	1.43	1.36		N/A	
Norway	1.44	1.39	1.41	1.40	1.38		-0.01	
Portugal (b)	1.46	1.64	1.55	1.57	1.58		0.02	
Bulgaria	1.37	1.38	1.40	1.37	1.63		0.05	
Belgium	1.71	1.67	1.60	1.67	1.63		-0.02	
Sweden	1.65	1.67	1.57	1.67	1.65		0.00	
Slovenia	1.56	1.55	1.61	1.68	1.69		0.04	↑
Estonia	2.00	1.79	1.81	1.74	1.70		-0.07	↓
Luxembourg	2.02	2.00	1.81	1.78	1.73		-0.08	↓
Ireland	1.76	1.79	1.66	1.91	1.83		0.03	
Croatia	1.97	1.79	1.85	1.90	1.87		-0.01	
Denmark	1.78	2.02	2.13	2.34	1.99		0.07	
EU/EEA	**1.95**	**2.03**	**2.00**	**2.04**	**2.06**		**0.02**	
Latvia	2.24	2.28	2.24	2.24	2.10		-0.03	
France	2.12	2.17	2.20	2.18	2.19		0.02	
Greece	1.90	2.00	2.11	2.14	2.39		0.11	↑
Italy	2.40	2.16	2.15	2.36	2.47		0.04	
Slovakia	2.02	2.30	2.47	2.40	2.49		0.10	
Finland (a)	2.79	2.77	2.64	2.50	2.52		-0.08	↓
United Kingdom		2.45	2.59	2.55	2.58		N/A	
Lithuania	2.39	2.39	2.35	2.54	2.59		0.06	
Malta	1.44	1.75	2.18	2.86	2.89		0.40	↑

(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, changes in the type of data or changes of sector for which data were reported (community versus total care data) between 2012 and 2016.

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

In 2016, consumption of carbapenems (ATC group J01DH) was 0.05 DDD per 1 000 inhabitants per day (Table D12). Between 2012 and 2016, 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 ten countries (Bulgaria, Croatia, Cyprus, Estonia, Hungary, Latvia, Lithuania, Malta, Romania and Slovakia). During the period 2012–2016, 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 2012–2016 (Table D13). A statistically significant increase was observed for nine countries (Bulgaria, Denmark, Greece, Italy, Hungary, Malta, Romania, Slovakia and Slovenia). During 2012–2016, France and Ireland showed a statistically significant decreasing trend.

The EU/EEA population-weighted mean consumption of piperacillin/tazobactam (ATC J01CR05) showed a statistically significant increasing trend for the period 2012–2016, as it did in most of the countries reporting hospital sector data.

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

In 2016, hospital consumption of oral vancomycin (ATC A07AA09) was reported from nine countries and ranged from 2×10^{-5} 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 22 countries, ranging from 2×10^{-6} DDD per 1 000 inhabitants per day in Estonia to 0.06 DDD per 1 000 inhabitants per day in the Finland. Metronidazole represented almost 100% of all nitroimidazole derivatives in the reporting countries.

Rifampicin (ATC J04AB02) consumption in 2016, reported in 19 countries, ranged from a minimum of 0.002 DDD per 1 000 inhabitants per day in Poland to a maximum of 0.17 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 the Table D14.

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

In 2016, 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 1.0 DDD per 1 000 inhabitants per day. The consumption varied by a factor of 8, ranging from 0.37 (Croatia) to 3.1 DDD per 1 000 inhabitants per day (Belgium).

In 2016, terbinafine (D01B02), fluconazole (J02AC01), and itraconazole (J02AC02) made up 73% 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 2016, 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 0.062 DDD per 1 000 inhabitants per day. Consumption varied by a factor of 8, from 0.022 DDD per 1 000 inhabitants per day (Poland) to 0.183 (Denmark).

In 2016, fluconazole (J02AC01) accounted for 55% 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 23% (Malta) to 94% (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 2016. The data are pooled across the two sectors (Table D17 and Figure D7). Austria, 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 3.0 DDD per 1 000 inhabitants per day. Country-specific consumption showed a 28-fold difference from 0.29 (Malta) to 7.4 (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) (0.9 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 53% 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 0.1% (Poland) to 85% (Estonia).

Malta reported the highest proportion of HIV/hepatitis B antivirals consumed (57%) and Greece reported the highest proportion of hepatitis B antivirals consumed (41%).

The proportion of hepatitis C antivirals consumed of the total consumption of antivirals for systemic use (ATC group J05) ranged from <0.01% (Italy) to 22% (Romania). In 2016, direct acting antivirals (DAA) were under surveillance within this group and 24 countries reported consumption of at least one DAA.

For herpes antivirals, the proportion of total consumption of antivirals for systemic use (ATC group J05) ranged from 0.03% (Italy) to 45% (Finland).

In 2016, 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 0.02% of the total consumption of antivirals for systemic use (ATC J05), to 0.36 DDD per 1 000 inhabitants per day in Latvia, accounting for 16% of the total consumption of antivirals for systemic use. Lithuania reported the highest proportion of consumption of anti-influenza substances (17%).

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 improve and measure the use of antimicrobials are the main elements of antimicrobial stewardship programmes at all levels.

Each year, EU/EEA countries report to ESAC-Net antimicrobial consumption data which 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 antibiotics use[1]. These quantity metrics and quality indicators should 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.

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 [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 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. For this report, the type of data reported from countries was the same as in the previous report (2015).

In 2016, consumption of antibacterials for systemic use (ATC group J01) in the community within the EU/EEA varied considerably between countries with a north-to-south gradient. There are many reasons for these large differences, some of which are cultural determinants [8]. This report shows that 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 2012–2016. Greece and Spain showed a statistically significant

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

increasing trend for the period 2012–2016, but statistically significant decreasing trends were observed for Finland, Luxembourg, Norway and Sweden.

Variations 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. The decrease in consumption expressed in the number of packages in some countries probably reflects a reduction in antibacterial prescriptions between 2012 and 2016, although this should be confirmed with national data from other sources. The indicator 'packages per 1 000 inhabitants per day' has disadvantages and there are concerns about its suitability for making country comparisons [9]. It may be useful as an additional metric for longitudinal monitoring of antibiotic consumption 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 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.

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 EU/EEA in 2016 it was 8.0 DDD per person per year. In other words, on average in 2016 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 just 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 [10]. 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, etc.).

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 (the number of tourists visiting Malta in 2016 was reported to be 3-4 fold higher than the Maltese population[2]). 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.

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

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

Carbapenems are the last-line group of antimicrobials and are mainly used in hospitals to treat patients with confirmed or suspected infections involving MDR gram-negative bacteria. 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

[2] https://nso.gov.mt/en/News_Releases/View_by_Unit/Unit_C3/Tourism_Statistics/Documents/2017/News2017_106.pdf

a few antibiotic groups, such as polymyxins, are available for the treatment of patients infected with such bacteria [9,14].

The second Join 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 resistance in *Klebsiella pneumoniae* isolates from invasive infections in EU/EEA countries reporting these data [15].

Although one third of the countries showed a statistically significant increase in carbapenem consumption, there was no statistically significant trend in the past five years at EU/EEA level overall.

Similarly, the latest data from the European Antimicrobial Resistance Surveillance Network (EARS-Net), 2016 show that population-weighted EU/EEA mean percentage of carbapenem resistance in *Klebsiella pneumoniae* isolates from invasive infections has been stable in recent years, with no significant trends [7].

Assuming that the average duration of carbapenem treatment is ten 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.

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

As expected, the consumption pattern of antimycotics and antifungals for systemic use in the hospital sector was different to that in the community due to different aetiology and variations in disease and disease severity treated in the sectors. 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. 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.

Public health implications

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 resistance patterns and trends differ across countries, so do the extent, pattern and trends of antimicrobial consumption. Thus, to understand antimicrobial resistance epidemiology in Europe requires reliable national antimicrobial consumption data.

Excessive antibiotic use in hospitals promotes the emergence and spread of multidrug-resistant bacteria responsible for healthcare-associated infections.

At the EU/EEA level 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 last-line antimicrobials, which is an indication for stronger stewardship measures 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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