

## SURVEILLANCE REPORT

### Annual Epidemiological Report for 2014

# **Antimicrobial consumption**

#### Key facts

- Thirty countries, including all EU Member States and two EEA countries (Iceland and Norway) reported data on antimicrobial consumption in the community (i.e. outside hospitals) and 23 countries reported these data for the hospital sector in 2014.
- 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: 10.6–35.1). During the period 2010–2014, no statistically significant change was observed. However, statistically significant decreasing trends were observed for Cyprus and Sweden, and a statistically significantly increasing trend was observed for the United Kingdom.
- In the hospital sector, the average consumption of antibacterials for systemic use was 2.0 DDD per 1 000 inhabitants per day (country range: 1.0–2.6) and this showed a statistically significant increasing trend during the period 2010–2014.
- The average consumption of carbapenems was 0.06 DDD per 1 000 inhabitants per day (country range: 0.02–0.14) and this showed a statistically significant increasing trend during the period 2010–2014. Statistically significant increasing trends were observed for six countries, while no country showed a statistically decreasing trend.
- The average consumption of polymyxins was 0.012 DDD per 1 000 inhabitants per day (country range: <0.001–0.095) and this did not show any statistically significant change during the period 2010–2014. However, a statistically significant increasing trend was observed for three countries.
- More detailed information is available in a comprehensive 2013–2014 ESAC-Net report at <u>https://ecdc.europa.eu/sites/portal/files/documents/Surveillance-antimicrobial-consumption-Europe-ESAC-Net-2013-14.pdf</u>

#### **Methods**

This report is based on data for 2014 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].

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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 surveillance data on antimicrobial consumption in humans reported by EU/EEA Member States to ECDC through the European Surveillance of Antimicrobial Consumption Network (ESAC-Net).

All 28 EU Member States and two EEA countries (Iceland and Norway) report antimicrobial consumption data annually to the European Surveillance System (TESSy) database. 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 2015 were used [4]. One DDD is the assumed 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 the ATC/DDD methodology enables different brands of medicines with different pack sizes and different strengths to be aggregated into units of measurement of active substances.

Three major categories of antimicrobials are under surveillance: 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).

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 this information was unavailable, as the number of DDD per ATC substance and route of administration.

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 denominator data on the total number of occupied bed-days are currently not available for most EU/EEA countries. In addition, presenting data with the same denominator enables cross-sectoral comparison.

For antibacterial consumption in the community, this report uses an additional indicator - 'packages per 1 000 inhabitants per day' for those countries which provided data on the number of packages consumed, according to the ATC index. This indicator only includes 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.

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 its 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 [5,6].

#### Antimicrobial consumption

In 2014, 30 countries, including all EU Member States and two EEA countries (Iceland and Norway) reported antimicrobial consumption for the community and 23 countries reported antimicrobial consumption for the hospital sector. Two countries (Cyprus and Romania) were only able to report data on total consumption in the country – i.e. without differentiating between the community and the hospital sector. For both the community and the hospital sector, consumption data were mainly on sales of antimicrobials in the country, or a combination of sales and reimbursement data.

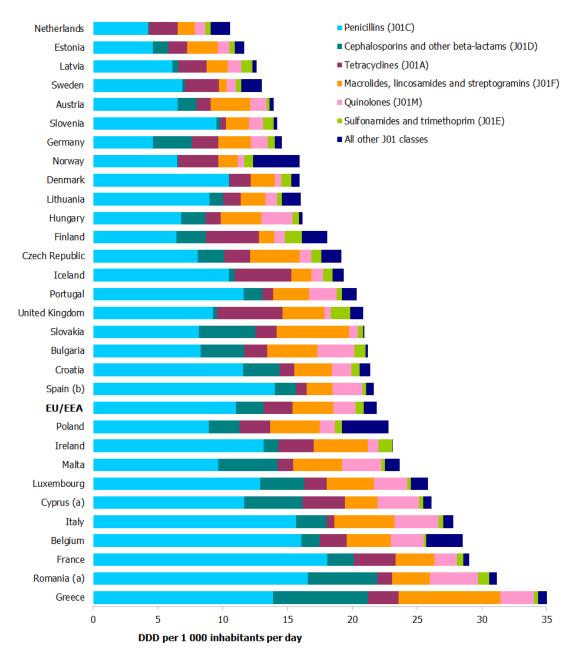
More details on reported European antimicrobial consumption data are available from the public ESAC-Net interactive database (data for 1997–2014) on the ECDC website.

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

#### Indicator: DDD per 1 000 inhabitants per day

In 2014, the EU/EEA population-weighted mean consumption of antibacterials for systemic use in the community was 21.9 DDD per 1 000 inhabitants per day. It ranged from 10.6 DDD per 1 000 inhabitants per day in the Netherlands to 35.1 DDD per 1 000 inhabitants per day in Greece (Figure 1).

## Figure 1. Consumption of antibacterials for systemic use (ATC group J01) and ATC group level 3 in the community, EU/EEA, 2014, 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.

Cyprus and Romania provided data on total consumption only, i.e. including both the community and the hospital sector. Data from these two countries are presented together with community consumption from other countries, because on average, 90% of the total consumption data correspond to consumption in the community.

As in previous years, penicillins were the most frequently consumed antibacterials in all countries, ranging from 32% (Germany) to 67% (Slovenia) of the total consumption in the community. The proportion of other antibacterial groups varied widely among countries – e.g. cephalosporins and other beta-lactams, from 0.2% (Denmark) to 21% (Slovakia); macrolides, lincosamides and streptogramins, from 5% (Sweden) to 27% (Slovakia); and quinolones, from 2% (United Kingdom) to 15% (Hungary) (Figure 1).

### Table 1. Trends in consumption of antibacterials for systemic use (ATC group J01) in the community, EU/EEA countries, 2010–2014, expressed as DDD per 1 000 inhabitants per day

Country	2010	2011	2012	2013		2014	Trends in antimicrobial	Average annual	Statistically significant trend
							consumption, 2010–2014	change 2010–2014	trend
Netherlands	11.2	11.4	11.3	10.8	10.6			-0.18	
Estonia	11.1	12.2	11.7	11.7	11.7			0.07	
Latvia	11.8	12.8	13.0	13.5	12.6			0.23	
Sweden	14.2	14.3	14.1	13.0	13.0		in ,	-0.36	
Austria	15.0	14.5	14.0	16.3	13.9		$\sim$	-0.04	•
Slovenia	14.4	14.4	14.3	14.5	14.2			-0.03	
Germany	14.1	13.9	14.8	15.7	14.6		$\sim$	0.28	
Norway	15.8	16.5	16.9	16.2	15.9			< 0.01	
Denmark	16.5	17.4	16.4	16.4	15.9			-0.21	
Lithuania	17.7*	19.0*	16.2	18.5	16.0			N/A	
Hungary	15.7	15.9	15.0	15.5	16.2			0.06	
Finland	18.5	20.1	19.5	18.3	18.1		~	-0.26	
Czech Republic	17.8	18.4	17.5	18.9	19.1		~	0.32	
Iceland	22.3*	22.3*	22.1*	21.9*	19.3			N/A	
Portugal	22.4	23.2	22.7	19.6*	20.3*		·	N/A	
United Kingdom	18.7	18.8	20.1	20.6	20.8			0.61	<b>↑</b>
Slovakia		23.8*	20.0	23.6	20.9		$\sim$	N/A	
Bulgaria	18.2	19.5	18.5	19.9	21.2			0.64	
Croatia	20.1	19.4	21.7	21.1	21.4		~~~	0.43	
Spain	20.3†	20.9†	19.7†	20.3†	21.6†			0.21	
EU/EEA	20.7	21.6	21.7	22.3	21.9			0.31	
Poland	19.0†	21.7†	22.9	23.6	22.8			N/A	
Ireland	20.3	22.6	23.0	23.8	23.1			0.68	
Malta	21.3	23.4	22.5	23.8	23.7		~~~	0.50	
Luxembourg	27.6	27.8	27.7	27.7	25.8			-0.36	
Cyprus	31.0*	32.0*	29.7*	28.2*	26.1*			-1.36	Ļ
Italy	27.9	28.2	27.5	28.6	27.8		$\sim$	0.03	
Belgium	28.4	29.0	29.8	29.6	28.5			0.08	
France	28.2	28.7	29.7	30.1	29.0			0.30	
Romania		30.9*	30.4*	31.6*	31.2*		$\sim$	N/A	
Greece	39.9*	35.7	32.5	32.2	35.1			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 2010 and 2014.

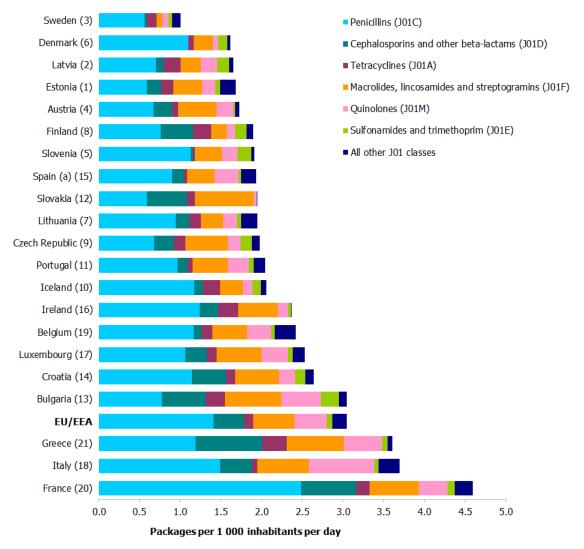
The symbols  $\uparrow$  and  $\checkmark$  indicate statistically significant increasing and decreasing trends, respectively.

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

The EU/EEA population-weighted mean consumption of antibacterials for systemic use in the community did not show any statistically significant trend during the period 2010–2014. Of the countries reporting comparable data for all years during the period 2010–2014, one (United Kingdom) showed a statistically significant increasing trend, and two countries (Cyprus and Sweden) showed a statistically significant decreasing trend.

#### Indicator: packages per 1 000 inhabitants per day

In 2014, 21 EU/EEA countries reported data on consumption for packages. The EU/EEA population-weighted mean consumption of antibacterials for systemic use in the community was 3.1 packages per 1 000 inhabitants per day and ranged from 1.0 packages per 1 000 inhabitants per day in Sweden to 4.6 packages per 1 000 inhabitants per day in France (Figure 2).



#### Figure 2. Consumption of antibacterials for systemic use (ATC group J01) and ATC group level 3 in the community, EU/EEA, 2014, expressed as packages per 1 000 inhabitants per day

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

The numbers in parentheses indicate the ranking of each of these 21 countries when community consumption of antibacterials for systemic use (ATC group J01) is expressed as DDD per 1 000 inhabitants per day (see Figure 3.1). EU/EEA refers to the corresponding population-weighted mean consumption based on the 21 countries that provided data.

The EU/EEA population-weighted mean consumption of antibacterials for systemic use in the community did not show any statistically significant change during the period 2010–2014 (Table 2). No country showed a statistically significant increase. A statistically significant decrease was observed for five countries (Denmark, Luxembourg, Slovenia, Spain and Sweden).

Country	2010	2011	2012 1.14	2013 1.05		2014	Trends in consumption of antibiotics, 2010–2014	Average annual change 2010–2014 -0.05	Statistically significant trend
Sweden	1.19	1.18			1.00				
Denmark	1.79	1.85	1.70	1.67	1.62			-0.05	Ļ
Latvia	1.59	1.73	1.70	1.76	1.65			0.01	
Estonia	1.70	1.82	1.77	1.74	1.68		·/	-0.01	
Austria	1.88	1.81	1.76	2.03	1.73		$\sim$	-0.01	
Finland	1.96	2.13	2.04	1.91	1.89		$\sim$	-0.04	
Slovenia	2.06	2.02	1.96	1.97	1.91			-0.03	$\downarrow$
Spain	2.13†	2.17†	2.01†	1.99†	1.93†			-0.06	$\downarrow$
Slovakia			2.53	3.02	1.94		$\sim$	N/A	
Lithuania			1.99	2.24	1.94			N/A	
Czech Republic	1.93	1.94	1.84	1.99	1.98		$\sim$	0.01	
Portugal	2.34	2.38	2.33	1.99†	2.04†			N/A	
Iceland					2.06		•	N/A	
Ireland	2.32	2.49	2.52	2.55	2.36			0.02	
Belgium	2.51	2.53	2.54	2.51	2.42			-0.02	
Luxembourg	2.83	2.74	2.68	2.67	2.53			-0.07	Ļ
Croatia	2.58	2.48	2.67	2.61	2.64		$\sim$	0.03	
Bulgaria	2.77	2.92	2.78	2.90	3.04			0.05	
EU/EEA	3.03	3.15	3.14	3.18	3.05		/	-0.04	
Greece		3.86	3.48	3.51	3.60		1	N/A	
Italy	3.84	3.78	3.70	3.83	3.70		$\sim$	-0.02	
France	4.82	4.86	4.86	4.85	4.59			-0.05	

## Table 2. Trends in consumption of antibacterials for systemic use (ATC group J01) in the community, EU/EEA, 2010–2014, expressed as packages per 1 000 inhabitants per day

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

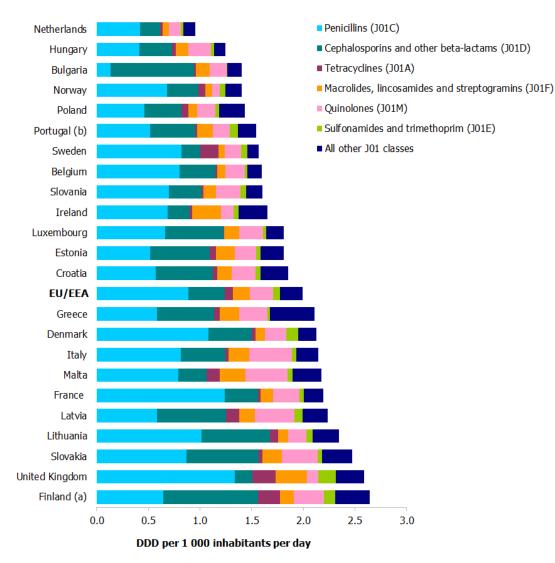
N/A = not applicable; linear regression was not applied due to missing data, changes in the type of data or changes of sector for which data were reported (community versus total care data) between 2010 and 2014.

The symbols  $\uparrow$  and  $\downarrow$  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 antibacterials for systemic use (ATC group J01) in the hospital sector

In 2014, 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. It ranged from 1.0 DDD per 1 000 inhabitants per day in the Netherlands to 2.6 DDD per 1 000 inhabitants per day in Finland (Figure 3). For the first time, Poland (2014) and the United Kingdom (2013, 2014) reported consumption data for the hospital sector.



### Figure 3. Consumption of antibacterials for systemic use (ATC group J01) in the hospital sector and ATC group, EU/EEA, 2014, 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 the 23 countries that provided data.

Variations in the relative proportions of consumption of antibacterial groups in hospitals were observed: 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 ranged from 3% in Sweden to 17% in Ireland; and consumption of quinolones ranged from 4% in the United Kingdom to 19% in Malta (Figure 3).

The EU/EEA population-weighted mean consumption of antibacterials for systemic use in the hospital sector showed a statistically significant increase during the period 2010–2014 (Table 3). A statistically significant increase was observed for Denmark while Belgium showed a statistically significant decrease.

## Table 3. Trends in consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, EU/EEA, 2010–2014, expressed as DDD per 1 000 inhabitants per day

Country	2010	2011	2012	2013	2014		Trends in antimicrobial consumption, 2010–2014	Average annual change 2010–2014	Statistically significant trend
Netherlands	1.06	0.97	0.96	0.95	0.95		· · · · ·	-0.02	
Hungary	1.33	1.20	1.23	1.20	1.25		Sar .	-0.02	
Bulgaria	1.40	1.41	1.37	1.38	1.40			0.00	
Norway	1.44	1.47	1.44	1.39	1.41			-0.01	
Poland					1.43		•	N/A	
Portugal (b)	1.41	1.45	1.46	1.64	1.55			0.05	
Sweden	1.51	1.60	1.65	1.67	1.57			0.02	
Belgium	2.02	2.02	1.71	1.67	1.60			-0.12	Ļ
Slovenia	1.72	1.66	1.56	1.55	1.61		~~~	-0.03	
Ireland	1.78	1.79	1.76	1.79	1.66			-0.03	
Luxembourg	2.08	2.02	2.02	2.00	1.81			-0.06	
Estonia	1.74	1.75	2.00	1.79	1.81			0.02	
Croatia	1.82	1.88	1.97	1.79	1.85			0.00	
EU/EEA	1.84	1.93	1.95	2.03	2.00			0.04	<b>↑</b>
Greece		2.00	1.90	2.00	2.11		$\sim$	N/A	
Denmark	1.75	1.74	1.78	2.02	2.13			0.10	î
Italy	2.10	2.23	2.40	2.16	2.15		$\sim$	0.00	
Malta	1.97	1.67	1.44	1.75	2.18		$\sim$	0.05	
France	2.23	2.12	2.12	2.17	2.20			< 0.01	
Latvia	3.10	2.34	2.24	2.28	2.24		\	-0.19	
Lithuania			2.39	2.39	2.35		~	N/A	
Slovakia			2.02	2.30	2.47			N/A	
United Kingdom (c)				2.45	2.59		/	N/A	
Finland (a)	2.83	3.09	2.79	2.77	2.64			-0.07	

(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.

(c) United Kingdom: data do not include consumption from UK-Northern Ireland

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 2010 and 2014.

The symbols  $\uparrow$  and  $\downarrow$  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 to treat patients with healthcare-associated infections caused by antimicrobial-resistant bacteria in the hospital sector

In 2014, the EU/EEA population-weighted mean consumption of carbapenems was 0.06 DDD per 1 000 inhabitants per day (Table 4). Between 2010 and 2014, it showed a statistically significant increasing trend. Similarly, a statistically significant increasing trend was observed for six countries (Bulgaria, Denmark, Hungary, Ireland, the Netherlands and Norway). None of the countries that reported data for all five years showed a statistically significant decreasing trend.

## Table 4. Trends in consumption of carbapenems (ATC group J01DH) in the hospital sector for EU/EEA countries, 2010–2014, expressed in DDD per 1 000 inhabitants per day

Country	2010	2011	2012	2012 2013 2014		Trends in consumption of carbapenems, 2010–2014	Average annual change 2010–2014	Statistically significant trend
Netherlands	0.015	0.018	0.019	0.020	0.019		0.001	<b>↑</b>
Bulgaria	0.010	0.013	0.013	0.014	0.020		0.002	<b>↑</b>
Poland					0.024	•	N/A	
Latvia	0.048	0.029	0.019	0.022	0.027		-0.005	
France	0.027	0.030	0.021	0.033	0.033	$\sim$	0.002	
Lithuania			0.026	0.026	0.033		N/A	
Hungary	0.026	0.027	0.032	0.037	0.042		0.004	Î
Slovakia			0.027	0.034	0.042		N/A	
Estonia	0.027	0.036	0.036	0.033	0.043		0.003	
Norway	0.044	0.044	0.045	0.046	0.047		< 0.001	Î
Sweden	0.052	0.052	0.054	0.056	0.053		< 0.001	
EU/EEA	0.046	0.048	0.053	0.060	0.059		0.004	Î
Belgium	0.068	0.079	0.062	0.062	0.064		-0.003	
Slovenia	0.067	0.078	0.074	0.061	0.066	$\sim$	-0.002	
United Kingdom (c)				0.061	0.069	/	N/A	
Croatia	0.055	0.058	0.065	0.060	0.073		0.004	
Italy	0.069	0.039	0.073	0.076	0.081	$\sim$	0.006	
Finland (a)	0.081	0.094	0.074	0.088	0.081	$\sim$	< 0.001	
Denmark	0.056	0.060	0.063	0.087	0.085		0.008	<b>↑</b>
Luxembourg	0.096	0.086	0.101	0.095	0.087	$\sim$	-0.001	
Malta	0.077	0.105	0.052	0.066	0.102	$\sim$	0.001	
Ireland	0.058	0.057	0.062	0.088	0.109		0.013	Î
Portugal (b)	0.141	0.140	0.143	0.146	0.139		<0.001	
Greece		0.130	0.133	0.135	0.143		N/A	

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

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

(c) United Kingdom: data do not include consumption from UK-Northern Ireland

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 2010 and 2014.

The symbols  $\uparrow$  and  $\downarrow$  indicate statistically significant increasing and decreasing trends, respectively.

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

In 2014, the EU/EEA population-weighted mean consumption of polymyxins was 0.012 DDD per 1 000 inhabitants per day (Table 5). It did not show any statistically significant change between 2010 and 2014. A statistically significant increasing trend was observed for three countries (Italy, Hungary and Norway). None of the countries reporting comparable data for all five years showed a statistically significant decreasing trend.

## Table 5. Trends in consumption of polymyxins (ATC group J01XB) in the hospital sector, EU/EEA countries, 2010–2014, expressed in DDD per 1 000 inhabitants per day

Country	2010	2011	2012	2013	2014		Trends in consumption of polymyxins, 2010–2014	Average annual change 2010–2014	Statistically significant trend
Finland (a)	0	0	0	0	0		· · · · · · · · · · · · · · · · · · ·	N/A	
Lithuania			0	0	0		•	N/A	
Norway	0.0001	0.0004	0.0006	0.0006	0.0006			< 0.001	1
Poland					0.001		•	N/A	
Latvia			0.003	0.002	0.001			< 0.001	
Sweden	0.001	0.001	0.001	0.001	0.001		1	< 0.001	
Bulgaria					0.002		•	N/A	
Netherland	0.005	0.003	0.002	0.003	0.002			-0,001	
Estonia	0.000	0.000	0.002	0.001	0.002			< 0.001	
Luxembourg	0.005	0.005	0.005	0.006	0.003			< 0.001	
Slovenia	0.001	0.002	0.004	0.003	0.005			0.001	
Denmark	0.002	0.002	0.002	0.004	0.006			< 0.001	
United Kingdom (c)				0.005	0.006			N/A	
Hungary	0.002	0.004	0.005	0.006	0.007			0.001	1
France	0.008	0.008	0.008	0.008	0.008			< 0.001	
Belgium	0.008	0.009	0.006	0.008	0.008		$\sim$	< 0.001	
Malta	0.026	0.004	0.002	0.006	0.011		· · · · ·	0.003	
EU/EEA	0.008	0.011	0.014	0.012	0.012			<0.001	
Ireland	0.014	0.014	0.015	0.015	0.013			< 0.001	
Portugal (b)	0.013	0.019	0.019	0.020	0.019			0.001	
Croatia	0.055	0.010	0.029	0.003	0.019		$\sim$	0.008	
Slovakia			0.020	0.023	0.025			N/A	
Italy	0.012	0.011	0.019	0.023	0.025			0.004	<b>↑</b>
Greece		0.078	0.085	0.084	0.095			N/A	
Romania	0.003						•	< 0.001	

(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.

(c) United Kingdom: data do not include consumption from UK-Northern Ireland

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 2010 and 2014.

The symbols  $\uparrow$  and  $\downarrow$  indicate statistically significant increasing and decreasing trends, respectively.

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

#### Discussion

EU/EEA 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 in evaluating the effects of such campaigns at national and international level.

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 are not included and neither are prescribed antimicrobials for which reimbursement was not claimed [7]. For this reason, countries that report reimbursement data and are known to have a substantial proportion of antimicrobials dispensed without a prescription are indicated in the tables and figures of this report. ESAC-Net will continue the joint analysis of sales and reimbursement data. A change of data provider and/or type of data could also introduce bias into the reported consumption rates. However, the number of countries that change data provider and/or types of data each year is small. In 2014, as in 2013, there were only two such changes: Poland and Romania reported sales data for the community, thus providing a more accurate estimate of national antimicrobial consumption since sales data include consumption without prescription and other non-reimbursed courses.

A standardised reporting protocol is essential to ensure comparability with other multinational surveillance networks. The ESAC-Net reporting protocol is built upon that of the former ESAC project. The WHO Regional Office for Europe recently established an antimicrobial consumption network collecting total care data (combined community and hospital sector) from non-EU/EEA, southern and eastern European countries (including Switzerland and Russia) [8]. These countries apply the same reporting protocol as ESAC-Net, which enables data comparability with EU/EEA countries.

In 2014, consumption of antibacterials for systemic use (ATC group J01) in the community in the EU/EEA varied considerably between countries with a north-to-south gradient. There are many reasons for the differences observed, some of which are cultural determinants [9]. This report shows that the EU/EEA population-weighted mean consumption of antibacterials for systemic use (ATC group J01) in the community did not change significantly during the period 2010–2014. Only five countries showed a statistically significant increase and one country showed a statistically significant decrease during 2010–2014. However, the trend analyses of sub-classes of antibacterials for systemic use revealed significant trends in the consumption of penicillins in over half of the countries included in the analyses. For example, the analyses indicated a shift in consumption of beta-lactamase-sensitive penicillins towards consumption of broad-spectrum antimicrobials - i.e. combinations of penicillins including beta-lactamase inhibitors (ATC group J01CR).

The antimicrobial consumption indicator 'packages per 1 000 inhabitants per day', is applied in 21 countries for community consumption of orally administered antibacterials for systemic use (ATC group J01). The changes 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 for antibacterials in antibacterial 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 antibiotic awareness campaigns where prescription data are not available.

A decrease in community antimicrobial consumption expressed in packages per 1 000 inhabitants per day in Denmark, Luxembourg, Slovenia, Spain and Sweden may represent a decrease in antimicrobial prescriptions for the period 2010 to 2014, although this should be confirmed with national data from other sources.

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.

For the hospital sector, the types of healthcare facilities included differ across EU/EEA countries. For example, data from Finland, the country with the second highest consumption of antibacterials for systemic use (ATC group J01) in the hospital sector in 2014, include consumption from nursing homes and remote primary healthcare centres. For this reason, data on the antimicrobial consumption in the hospital sector in Finland should be interpreted with caution when compared to that of other countries.

In contrast to prescribing practices in the community, penicillins were not the most frequently prescribed antibacterial subclasses in the hospital sector for all countries, and the proportions of cephalosporins, other betalactams (including carbapenems) and other groups of antimicrobials were generally higher than in the community.

The prevalence of antimicrobial-resistant microorganisms, including multi drug-resistant (MDR) strains, is increasing, especially in hospitals where selective antimicrobial pressure is present. Treating infections caused by

these bacteria has become a serious public health problem as there are fewer, or sometimes no, effective antimicrobial agents available.

Patients receiving antimicrobials are more likely to become colonised with antimicrobial-resistant bacteria - and therefore are at greater risk of developing subsequent infections with these bacteria - than patients who do not receive antimicrobials. Antimicrobial-resistant bacteria are transmitted from patient to patient and the more they are exposed, the greater the bacterial selection pressure will be, subsequently causing them to develop even greater antimicrobial resistance. The spread of antimicrobial-resistant bacteria in healthcare facilities has become a public health threat. One significant driver for the selection of highly antimicrobial-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, the broadest spectrum antibacterials, are a last-line group of antimicrobials and are mainly used in hospitals to treat patients with confirmed or suspected infections involving MDR gram-negative bacteria [10,11].

Assuming that the average duration of carbapenem treatment is 10 days, the consumption of 0.06 DDD per 1 000 inhabitants per day corresponds to more than one million carbapenem prescriptions issued in the EU/EEA each year.

The latest data from the European Antimicrobial Resistance Surveillance Network (EARS-Net) show a significant increase in the population-weighted EU/EEA mean percentage of carbapenem resistance in *Klebsiella pneumoniae* isolates from invasive infections. The increasing spread of carbapenem-resistant *Enterobacteriaceae* (mostly *Klebsiella pneumoniae*) has been confirmed in a recent survey of national experts from 38 European countries.

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 these bacteria.

#### Public health conclusions

Antimicrobial resistance is a serious threat to public health in the EU/EEA and antimicrobial consumption is one of the main drivers of antimicrobial resistance.

Some countries have succeeded in reducing consumption in the community when measured in packages, although the overall number of packages (a proxy for prescriptions) has remained stable.

The spread of multidrug-resistant bacteria in healthcare facilities has become a public health threat. One significant driver for the selection of multidrug-resistant bacteria responsible for healthcare-associated infections in hospitalised patients is the use of specific, mostly reserve or last-line antimicrobials in hospitals.

It is a major concern that in the hospital sector across the EU/EEA, the consumption of last-line groups of antimicrobials, such as carbapenems, has increased. On the one hand, if prescribed inappropriately, this may lead to critical situations with a lack of effective treatment options for patients with bacterial infections, but on the other hand, it may indicate that the spread of MDR bacteria has reached a level at which other antibacterials have become ineffective.

The rational use of last-line antimicrobials should be a high priority in national antimicrobial stewardship programmes.

#### References

- 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: <u>https://ecdc.europa.eu/en/annual-epidemiological-reports-2016/methods</u>.
- European Centre for Disease Prevention and Control. Surveillance systems overview [internet, downloadable spreadsheet]. Stockholm: ECDC; 2018. Available from: <u>https://ecdc.europa.eu/en/publicationsdata/surveillance-systems-overview-2016</u>
- 3. European Centre for Disease Prevention and Control. Surveillance atlas of infectious diseases [internet]. Stockholm: ECDC; 2017 [cited 30 Jan 2018]. Available from: <u>http://atlas.ecdc.europa.eu/public/index.aspx</u>]
- 4. WHO Collaborating Centre for Drug Statistics Methodology. ATC Index with DDDs. Oslo, WHO 2018 Available from: <u>https://www.whocc.no/atc\_ddd\_index/</u>
- 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 <u>http://ecdc.europa.eu/en/publications/Publications/antimicrobial-consumption-europe-esac-net-2012.pdf</u>
- European Centre for Disease Prevention and Control. Antimicrobial consumption (AMC) reporting protocol 2016. European Antimicrobial Resistance Surveillance Network (EARS-Net) surveillance data for 2015 Available from <u>https://ecdc.europa.eu/sites/portal/files/documents/antimicrobial-consumption-reportingprotocol.pdf</u>
- Safrany N, Monnet DL. Antibiotics obtained without a prescription in Europe. Lancet Infect Dis. 2012 Mar;12(3):182-3
- 8. Borg MA. Cultural determinants of infection control behaviour: understanding drivers and implementing effective change. J Hosp Infect. 2014 Jan 14.
- Versporten A, Bolokhovets G, Ghazaryan L, Abilova V, Pyshnik G, Spasojevic T, et al. Antibiotic use in eastern Europe: a cross-national database study in coordination with the WHO Regional Office for Europe. Lancet Infect Dis. 2014 Mar 20, <u>http://dx.doi.org/10.1016/S1473-3099(14)70071-4</u>
- European Centre for Disease Prevention and Control. Systematic review of the effectiveness of infection control measures to prevent the transmission of carbapenemase-producing Enterobacteriaceae through crossborder transfer of patients. Stockholm: ECDC; 2014
- 11. EUROROUNDUPS. Carbapenemase-producing *Enterobacteriaceae* in Europe: assessment by national experts from 38 countries. Euro Surveill. 2015;20(45):pii=30062. DOI: <u>http://dx.doi.org/10.2807/1560-7917.ES.2015.20.45.30062</u>