ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

SURVEILLANCE REPORT

Surveillance of antimicrobial consumption in Europe

2012

www.ecdc.europa.eu

ECDC SURVEILLANCE REPORT

Surveillance of antimicrobial consumption in Europe

2012

This report of the European Centre for Disease Prevention and Control (ECDC) was coordinated by Klaus Weist.

Contributing authors
Klaus Weist, Arno Muller, Dominique Monnet and Ole Heuer
Data analysis: Klaus Weist and Arno Muller.

Acknowledgements
The ESAC-Net Coordination Group members: Milan Čižman, Samuel Coenen, Herman Goossens, Kari Grave, Danilo Lo Fo Wong, Mike Sharland, Arno Muller, Hege Salvesen Blix, Arjana Tambić Andrasevic, Rolanda Valintėlienė, Theo Verheij, Hayley Wickens and Peter Zarb are acknowledged for providing valuable comments and scientific advice during the production of the report.

All ESAC-Net participants and National Coordinators are acknowledged for providing data and valuable comments for this report.

Gaetan Guyodo, Dana Ursut and Catalin Albu are acknowledged for data management and providing technical support to the participating countries.

Suggested citation: European Centre for Disease Prevention and Control. Surveillance of antimicrobial consumption in Europe 2012. Stockholm: ECDC; 2014.

Stockholm, September 2014

ISBN 978-92-9193-589-5

doi 10.2900/32937

Catalogue number TQ-AT-14-002-EN-N

Contents

Figures

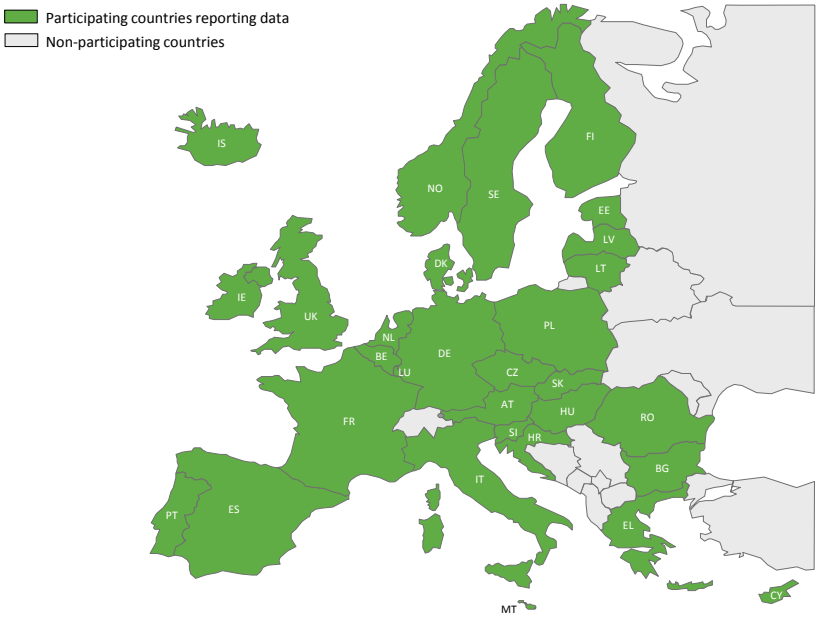
Tables

Abbreviations

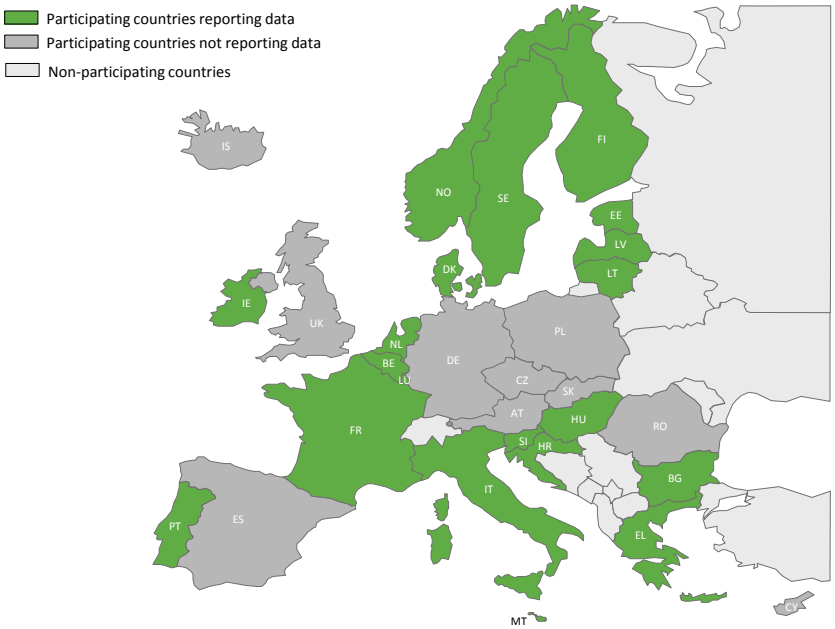
ARPEC project	Antibiotic Resistance and Prescribing in European Children project
ATC classification	Anatomical Therapeutic Chemical classification
DDD	Defined daily dose
EARS-Net	European Antimicrobial Resistance Surveillance Network
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
ESAC project	European Surveillance of Antimicrobial Consumption project
ESVAC project	European Surveillance of Veterinary Antimicrobial Consumption project
EU	European Union
Eurostat	Statistical Office of the European Union
HAI-Net	Healthcare-associated Infections Surveillance Network
TESSy	The European Surveillance System, at ECDC
WHO	World Health Organization

EU/EEA countries participating in ESAC-Net, 2012

Community antimicrobial consumption: EU/EEA countries reporting for 2012



Hospital sector antimicrobial consumption: EU/EEA countries reporting for 2012



AT	Austria	EL	Greece	IT	Italy	PT	Portugal
BE	Belgium	ES	Spain	LT	Lithuania	RO*	Romania
BG	Bulgaria	FI	Finland	LU	Luxembourg	SE	Sweden
CY*	Cyprus	FR	France	LV	Latvia	SI	Slovenia
CZ	Czech Republic	HR	Croatia	MT	Malta	SK	Slovakia
DE	Germany	HU	Hungary	NL	Netherlands	UK	United Kingdom
DK	Denmark	IE	Ireland	NO	Norway		
EE	Estonia	IS*	Iceland	PL	Poland		

*: Cyprus, Iceland and Romania provided total care data, i.e. including the hospital sector.

National institutions/organisations participating in ESAC-Net

Country	National institutes/organisations	Website
Austria	Ministry of Health	www.bmg.gv.at/
Belgium	Public Health, Food Chain Safety and Environment Scientific Institute of Public Health University of Antwerp (Laboratory of Medical Microbiology) National Institute for Health and Disability Insurance (INAMI-RIZIV)	www.health.belgium.be www.wiv-isp.be www.ua.ac.be www.inami.fgov.be/homefr.htm
Bulgaria	National Centre of Infectious and Parasitic Diseases Alexander University Hospital, Medical University	www.ncipd.org
Croatia	Croatian Academy of Medical Sciences Interdisciplinary Section for Antibiotic Resistance Control (ISKRA), Ministry of Health	www.Iskra.bfm.hr
Cyprus	Directorate of Medical and Public Health Services Pharmaceutical Services	www.moh.gov.cy
Czech Republic	Charles University, Faculty of pharmacy	www.faf.cuni.cz
Denmark	Statens Serum Institut	www.ssi.dk
Estonia	Health Board State Agency of Medicines	www.terviseamet.ee www.ravimiamet.ee
Finland	National Institute for Health and Welfare	www.thl.fi
France	National Institute for Public Health Surveillance Agency for the Safety of Health Products	www.invs.sante.fr www.ansm.sante.fr/
Germany	Robert Koch Institute Wissenschaftliches Institut der AOK (WIdO)	www.rki.de www.wido.de
Greece	Hellenic Centre for Disease Control and Prevention National Organization for Medicines	www.keelpno.gr www.eof.gr
Hungary	National Centre for Epidemiology University of Szeged	www.oek.hu www.u-szeged.hu
Iceland	Centre of Health Security and Communicable Disease Control	www.landlaeknir.is/ www.lyfjastofnun.is/
Ireland	Health Protection Surveillance Centre	www.hpsc.ie
Italy	Ministry of Health National Institute of Health Italian Medicines Agency	http://www.salute.gov.it www.simi.iss.it www.agenziafarmaco.gov.it
Latvia	The Centre for Disease Prevention and Control (CDPC) of Latvia State Agency of Medicines of Latvia	www.spkc.gov.lv www.vza.gov.lv
Lithuania	Institute of Hygiene	www.hi.lt
Luxembourg	Ministry of Health	www.ms.public.lu/fr/index.html
Malta	National Antibiotic Committee	www.nacmalta.info/
Netherlands	National Institute for Public Health and the Environment Dutch working group on antibiotic policy	www.rivm.nl www.swab.nl
Norway	Norwegian Institute of Public Health	www.fhi.no
Poland	Ministry of Health National Institute of Public Health National Medicines Institute	www.mz.gov.pl www.pzh.gov.pl www.il.waw.pl
Portugal	National Authority of Medicines and Health Products	www.infarmed.pt
Romania	National Institute of Public Health	www.insp.gov.ro.
Slovakia	Comenius University	www.uniba.sk

Country	National institutes/organisations	Website
Slovenia	National Institute of Public Health University Medical Centre Ljubljana	www.ivz.si/ www.4.kclj.si
Spain	National Centres of Microbiology and Epidemiology Spanish Agency of Medicines and Medical Devices (AEMPS) University Hospital Son Espases University Hospital of Bellvitge	www.aemps.gob.es www.hospitalsonespases.es/ www.bellvitgehospital.cat
Sweden	Public Health Agency of Sweden	http://www.folkhalsomyndigheten.se/
United Kingdom	Public Health England Health Protection Scotland Public Health Agency University of Dundee University Hospital of South Manchester Public Health Wales The British Society for Antimicrobial Chemotherapy	www.hpa.org.uk www.hps.scot.nhs.uk www.dundee.ac.uk www.uhsm.nhs.uk www.wales.nhs.uk www.bsac.org.uk

Summary

This is the third annual report of the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) published by ECDC. The report is based on antimicrobial consumption data from the community (primary care sector) and the hospital sector reported to ECDC for the year 2012 by 28 EU Member States and two EEA non-EU countries (Iceland and Norway).

Key findings

In the **community**, i.e. outside hospitals, consumption of antibacterials for systemic use (Anatomical Therapeutic Chemical (ATC) group J01) in 2012 was reported by 30 countries. Consumption varied by a factor of 2.8 between the highest consumption (31.9 defined daily doses (DDD) per 1 000 inhabitants and per day in Greece) and the lowest (11.3 DDD per 1 000 inhabitants and per day in the Netherlands). The population-weighted EU/EEA mean consumption was 21.5 DDD per 1 000 inhabitants and per day and no significant trends in the mean consumption are apparent for the last 5 years.

The most commonly used subgroups of antibacterials were the combinations of penicillins including beta-lactamase inhibitors (ATC group J01CR) and penicillins with extended-spectrum (ATC group J01CA), followed by macrolides (ATC group J01FA) and tetracyclines (ATC group J01AA). The largest increase in consumption of antibacterials for systemic use in the community was seen in the United Kingdom, increasing from 18.8 DDD per 1 000 inhabitants and per day in 2011, to 20.1 DDD per 1 000 inhabitants and per day in 2012. Greece and Poland reported a 9% decrease in the consumption from 35.1 and 21.9 DDD per 1 000 inhabitants and per day in 2011 to 31.9 and 19.8 DDD per 1 000 inhabitants and per day in 2012, respectively. A trend analysis performed on data on consumption of antibacterials for systemic use for the period 2008–2012 and including 22 ESAC-Net participating countries, showed a significant increase for five countries (Belgium, Latvia, Norway, Spain and the United Kingdom). A significant decrease was observed for Austria.

For antibacterials for systemic use (ATC group J01) that are administered orally, ESAC-Net also reported consumption as a number of packages per 1 000 inhabitants and per day. In 2012, consumption of these antibacterials ranged from 1.1 packages per 1 000 inhabitants and per day (Sweden) to 4.9 packages per 1 000 inhabitants and per day (France). On average, 3.1 packages of antibacterials for systemic use (ATC group J01) were consumed per 1 000 inhabitants and per day. A few countries (Belgium, Bulgaria, Denmark and Portugal) moved up or down in the ranking by three or more places when consumption was expressed in packages per 1 000 inhabitants and per day instead of DDD per 1 000 inhabitants and per day.

In 2012, 25 countries reported data on consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01BA) in the community. Consumption varied by a factor of 7.2 between the highest consumption (3.3 DDD per 1 000 inhabitants and per day in Belgium) and the lowest (0.46 DDD per 1 000 inhabitants and per day in Malta). Terbinafine, ketoconazole, fluconazole and itraconazole accounted for 98% of the total antimycotic and antifungal consumption in the community in all countries. Terbinafine consumption accounted for more than 50% of the total systemic antimycotic and antifungal consumption in 18 (72%) countries.

In 2012, the 12 consensus-based quality indicators from the former ESAC project, used to express data on consumption of antibacterials for systemic use (ATC group J01) in the community [1-2] showed a distinct variation across Europe. Significant and divergent trends were observed for the two quality indicators measuring consumption of beta-lactamase-sensitive penicillins and combinations of penicillins including beta-lactamase inhibitors:

- Consumption of beta-lactamase-sensitive penicillins (ATC group J01CE) expressed as a percentage of the total consumption of antibacterials for systemic use (ATC group J01), varied from <0.1% in Italy to 27.7% in Sweden and 27.9 % in Denmark. A trend analysis revealed a significant decrease in 11 countries (Austria, Belgium, Bulgaria, Denmark, Estonia, Italy, Latvia, Luxembourg, the Netherlands, Norway and Spain) for this indicator between 2008 and 2012.
- Conversely, 10 countries (Austria, Denmark, Estonia, France, Germany, Ireland, Italy, Luxembourg, Slovenia and the United Kingdom) saw a significant increase in their consumption of combinations of penicillins including beta-lactamase inhibitors (ATC group J01CR) expressed as a percentage of the total consumption of antibacterials for systemic use.

Further, the consensus-based quality indicator which defines the ratio of the consumption of broad-spectrum penicillins/cephalosporins/macrolides to that of narrow-spectrum penicillins/cephalosporins/macrolides [1-2] also showed large variation; from 0.2 in Sweden and Norway to 258.3 in Greece.

In the **hospital sector**, consumption of antibacterials for systemic use (ATC group J01) data varied from 1.0 DDD per 1 000 inhabitants and per day in the Netherlands, to 2.8 in Finland. The population-weighted EU/EEA mean consumption was 2.0 DDD per 1 000 inhabitants and per day and no significant trends in the mean consumption are apparent for the last five years. The most frequently used subgroup in the hospital sector was penicillins (ATC group

J01C), followed by other beta-lactam antibacterials including cephalosporins (ATC group J01D) and quinolones (ATC group J01M). A trend analysis performed on data on consumption of antibacterials for systemic use for the period 2008–2012 and including 11 ESAC-Net participating countries, showed a significant decrease for Bulgaria.

In 2012, 18 countries reported data on consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01BA) in the hospital sector, ranging from 0.03 DDD per 1 000 inhabitants and per day in Lithuania to 0.2 DDD per 1 000 inhabitants and per day in Denmark. Overall, amphotericin B and fluconazole accounted for 71% of the total antimycotic and antifungal consumption in the hospital sector in participating countries. Fluconazole consumption alone accounted for more than 50% of the total systemic antimycotic and antifungal consumption in 11 (61%) of these countries.

In 2012, data on total antiviral consumption (ATC group J05), jointly presented for both the community and the hospital sector, were available from 24 countries. Consumption varied by a factor of 11 between the highest (4.4 DDD per 1 000 inhabitants and per day in Portugal) and the lowest consumption (0.1 DDD per 1 000 inhabitants and per day in Malta). Based on indications for treatment with antivirals in ATC group J05, as suggested by the former ESAC project [3], most antivirals reported were 'HIV/AIDS antivirals' followed by 'herpes antivirals'. Latvia showed a different pattern with the highest consumption among ESAC-Net participants being of antivirals active against influenza.

Conclusions

The results presented in this report document trends of antimicrobial consumption across Europe. The 2012 EU/EEA population-weighted mean consumption of antibacterials for systemic use (ATC group J01) in the community was at the same level as that of 2011 and only five countries showed a significant increase over the five-year period ending in 2012. However, one country, Greece, having the highest consumption figures, showed a remarkable decrease in the consumption of antibacterials for systemic use between 2011 and 2012. The decrease coincided with the implementation of an electronic prescription system at the end of 2010. For the hospital sector, the 2012 EU/EEA population-weighted mean consumption of antibacterials for systemic use (ATC group J01) as well the corresponding national figures were similar to those of previous years and no significant trend can be observed in the consumption for the period 2008–2012.

When analysing the data at ATC subgroup levels, significant, but divergent, trends were observed in both sectors, highlighting an increase in consumption of some groups of antibacterials at the expense of others. For instance there is a significant increase in the ratio of broad-spectrum penicillins/cephalosporins/macrolides to narrow-spectrum penicillins/cephalosporins/macrolides consumed in the community (consensus-based quality indicators as defined by the former ESAC project) over the last 5-year period, 2008–2012, in two thirds of the countries. It is difficult to identify the factors and reasons behind these changes without additional data on prescriptions. However, the inclusion of the number of packages per 1000 inhabitants and per day may provide a basis for an estimate of the number of prescription [4]. Combining the additional indicator on packages with the indicator of DDD per 1000 inhabitants and per day may provide a more appropriate assessment of interventions, e.g. national awareness campaigns. Detailed information on national programmes and campaigns on the prudent use of antimicrobials is needed before conclusions can be drawn about which factors may have influenced the trends.

In 2012, participation in reporting data for the hospital sector improved, with three more countries reporting than in 2011. However, two of these countries (Slovakia and Croatia) were already able to report hospital consumption data to the former ESAC project in 2009. ESAC-Net aims to obtain hospital sector data from all network participants though this is currently not the case; a number of countries cannot provide separate hospital consumption data as defined in the reporting protocol. To further increase the number of countries reporting antimicrobial consumption data for the hospital sector ESAC-Net is developing an EU-wide protocol for collecting data at the hospital level and by using additional denominators for hospital consumption. Such developments should help to identify areas for improvement, to be addressed by national, regional and local antimicrobial stewardship programmes.

Inter-country comparisons using the results presented in this report should be made with caution, as certain countries report their total consumption while most other countries only report data on the community consumption. In addition, reporting practices may vary from year to year even in the same country. Finally, there are differences in the sources of national data and in the availability of national registries of all antimicrobials available on the market in each country; the latter being a prerequisite for presenting comparable data on antimicrobial consumption.

ESAC-Net will continue to collect, analyse and report data from EU/EEA countries, both in the community and in the hospital sector, and provide independent reference information on antimicrobial consumption in Europe. At the European level, the data provided can facilitate the adoption of national targets by Member States to reinforce best practice for the use of antimicrobials.

ECDC provides public access to the ESAC-Net database at the 4th level of the ATC classification in this annual report and in an interactive database on the ECDC website [5], where country overview sheets summarising national results are also provided.

1 Introduction

The use and overuse of antimicrobials is one of the main factors responsible for the development and spread of antimicrobial resistance. This has become a serious threat to public health, notably because of the emergence and spread of highly resistant bacteria, and because there are very few novel antimicrobial agents in the research and development pipeline. European countries increasingly implement, or plan to implement, actions to control antimicrobial resistance in the community through rational use of antimicrobials, including awareness campaigns on the prudent use of antibiotics. Information on antimicrobial consumption in Europe, and in particular the consumption of antibacterials, can be an important source for healthcare professionals and policy makers monitoring progress towards a more prudent use of antibiotics.

This report is based on antimicrobial consumption data from the community (primary care sector) and the hospital sector reported to ECDC for the year 2012 by 28 EU Member States and two EEA non-EU countries (Iceland and Norway).

It includes data for three major categories of antimicrobials:

- antibacterials for systemic use (ATC group J01);
- antimycotics for systemic use and antifungals for systemic use (ATC groups J02 & D01BA);
- antivirals for systemic use (ATC group J05).

The largest proportion of the antimicrobial consumption by humans takes place in the community, i.e. outside of hospitals. Each sector of the healthcare system, i.e. the community and hospital sectors, typically care for different types of patients. Thus, the typical patterns of antimicrobial consumption differ between these sectors. That is why results of consumption of antimicrobials of the ATC groups J01, J02 & D01BA are presented separately for the two sectors.

However, consumption of antivirals for systemic use (ATC group J05) is reported for both sectors grouped together. This is because in several countries, certain antiviral classes even for primary care can only be dispensed in a hospital, while in other countries such antivirals are mostly dispensed in community pharmacies.

Two quantitative indicators are used to report antimicrobial consumption, the number of DDD per 1 000 inhabitants and per day, and the number of packages per 1 000 inhabitants and per day.

The former ESAC project developed 12 quality indicators for antimicrobial consumption in the community based on a consensus of European antimicrobial surveillance experts [2]. It was concluded that these indicators could be used to better describe antimicrobial consumption and to assess changes in national antibiotic prescribing patterns in Europe. The indicators report: consumption expressed in DDD per 1 000 inhabitants and per day for ATC group J01 and as a percentage of the total consumption of antibacterials for systemic use (ATC group J01) corresponding to various subgroups; the ratio of the consumption of broad-spectrum and narrow-spectrum antibacterials (as defined by Coenen, et al [2]); and seasonal variations of the total consumption of antibacterials for systemic use. When comparing results of different countries for the 12 quality indicators, low values of the indicators suggest better quality, with the best quality being within the first quartile (p0–p25). Values within the second quartile (i.e. p25–p50) suggest better quality than values of indicators in the third quartile, etc. Only the indicator describing the percentage of the total consumption of antibacterials for systemic use (ATC group J01) corresponding to the subgroup of beta-lactamase-sensitive penicillins is evaluated in the opposite way, i.e. high values of the indicator suggest better quality with the best quality being within the fourth quartile (p75–p100). This report presents the results of the quality indicators for 2012 consumption data.

European surveillance of antimicrobial consumption

ESAC-Net

ESAC-Net is the continuation of the former ESAC project (managed by the University of Antwerp until June 2011) and is a Europe-wide network of national surveillance systems providing independent reference data on antimicrobial consumption in Europe, reported by 30 EU/EEA countries. It collects and analyses data from the community (primary care) and the hospital sector.

The former ESAC project included point prevalence surveys of antimicrobial use conducted in 2008 and 2009 in acute care hospitals and in nursing homes across EU countries. These point prevalence surveys are now included as part of the activities of the Healthcare-Associated Infections Surveillance Network (HAI-Net) at ECDC [6] and data from European acute care hospitals in 2011–2012 are provided through the ECDC point prevalence survey of healthcare-associated infections and antimicrobial use. Data from long-term care facilities are collected by the ECDC-funded project 'Healthcare-associated Infections and Antimicrobial Use in European Long-Term Care Facilities (HALT-2)'.

The objectives of ESAC-Net are:

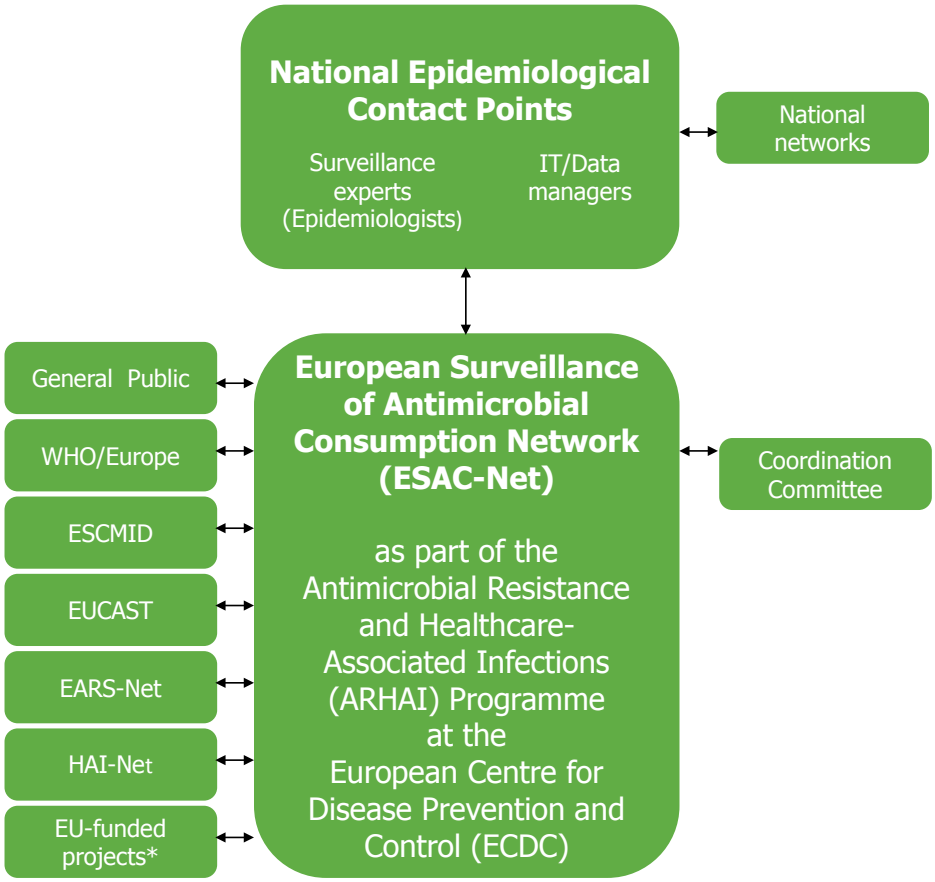
- to provide continuous surveillance of antimicrobial consumption in the European Union;
- to work towards comparable surveillance methods in the community and in the hospital sector;
- to analyse inter-country differences and provide regular feedback to participating Member States;
- to provide public access to information on antimicrobial consumption via the ESAC-Net interactive database [5].

To maintain and facilitate data reporting, ECDC ensures:

- validation of community (primary care) and hospital sector data;
- analysis of the trends in antimicrobial consumption overall and in the different ATC groups;
- public access to information on antimicrobial consumption in Europe through an interactive database;
- timely information and feedback to EU/EEA countries on indicators of antimicrobial consumption. These indicators provide a basis for monitoring the progress of EU/EEA countries towards prudent use of antimicrobials.

Figure 1.1 illustrates how the network was organised in 2012. Experts in antimicrobial consumption were nominated by each country to become network participants and they are supported by a coordination group. This group comprises representatives from ESAC-Net participating countries and members of the management team and advisory board of the former ESAC project. There are also observers in the coordination group from other EU projects including 'European Surveillance of Veterinary Antimicrobial Consumption (ESVAC)' and 'Antibiotic Resistance and Prescribing in European Children (ARPEC)'. This coordination group discusses technical, epidemiological and other scientific aspects of antimicrobial consumption surveillance and makes suggestions to ECDC in order to further develop the network and improve its effectiveness.

Figure 1.1. Organisation of ESAC-Net (2012)



** EU-funded projects on antimicrobial consumption, e.g. ARPEC and ESVAC.*

2 Technical notes

2.1 Terminology and definitions

The term 'antimicrobial consumption' is used in this report whereas 'antimicrobial use' is applied to data from the point prevalence surveys in acute care hospitals and in long-term-care facilities where data on the actual application of antimicrobials are retrieved from patient charts. These two ECDC point prevalence surveys are now part of HAI-Net.

The term 'community' is used to designate the sector providing mainly primary care (general practitioner, specialists) outside of hospitals. The terms 'ambulatory care' and 'outpatient sector' were not used to avoid potential misinterpretations as being patient care in hospitals or other healthcare facilities that did not require the patient to stay overnight.

Antimicrobial consumption is expressed as a number of DDD per 1 000 inhabitants and per day. Complementary to this measurement unit, the number of packages per 1 000 inhabitants and per day is also used, provided that the country collects and reports data at the package level. Because the ATC/DDD system cannot take into account changes in package content, information on the sales of packages is deemed to improve the understanding and interpretation of differences in the levels and trends of consumption observed within countries and between countries.

Antimicrobials are grouped according to the Anatomical Therapeutic Chemical (ATC) classification. The 2013 version of the ATC/DDD index from the WHO Collaborating Centre for Drug Statistics methodology (Oslo, Norway) was applied. The latest ATC/DDD index is available at www.whocc.no/atc_ddd_index and contains all valid ATC codes and corresponding DDD. Changes between different ATC/DDD indexes (e.g. between 2013 and 2014) can also be found there. The three major groups of antimicrobials considered in this report (ATC groups J01, J02 & D01BA, J05) are often referred to by their ATC codes rather than the name of the group or the active ingredients.

The group of antimicrobials 'antibacterials for systemic use' (ATC group J01) are often referred to by the public as 'antibiotics'. However, the term 'antibiotics' defining substances produced by one microorganism and specifically inhibiting the growth of others would also include agents such as topical antibacterials for which data are not collected by ESAC-Net and even antifungals, so throughout this report the term 'antibacterials for systemic use' has been used to refer to this group of antimicrobials.

In addition to the ATC classification, for two groups of antibacterials for systemic use, i.e. macrolides and quinolones, and for antivirals, further sub-classifications were used that are not supported by the ATC classification. These were introduced by the ESAC project [3, 7-8] and updated for new ATC codes and changes published by the WHO Collaborating Centre for Drug Statistics methodology (Annex 1).

2.2 Data collection and reporting for 2012

Data on antimicrobial consumption were collected for the community (primary care sector) and for the hospital sector, and for some countries aggregated data for both sectors were combined (total care), according to the 2013 reporting protocol [9].

For the first time, Croatia was eligible to report antimicrobial consumption data to ESAC-Net.

The ESAC-Net metadata [9] are, for most variables, based on the ESAC project core data. In November 2011, training was provided for the ESAC-Net participants on how to prepare, upload and approve their national consumption data. The call for 2012 surveillance data started in March 2013 and was open until 30 June 2013. After uploading, each country approved its own data and the results made available from the ECDC website.

There are two options for reporting ESAC-Net data to ECDC:

- The preferred standard option, i.e. reporting of national antimicrobial consumption data at the medicinal product level and expressed as a number of packages sold. For this option, a valid national register of available antimicrobials is required (national registry data).
- A 'light' version, i.e. when national registry data are not available, reporting of aggregated numbers of DDD from national antimicrobial consumption data at the ATC substance level.

Additionally, ESAC-Net encouraged participants to report data on the above variables by age group, gender and type of prescriber, as well as to report quarterly rather than yearly data.

2.3 Data validation and analysis

The ESAC-Net data validation process consists of three steps:

- During upload of the national data, a first quality check of the data is performed by The European Surveillance System (TESSy) using its in-built validation rules for the ESAC-Net metadata [9]. Following the data upload, each country approves its own data.
- As a second step, each country checks its own data for consistency by comparing data displayed in TESSy online reports with data from national sources.
- ESAC-Net experts and TESSy data managers perform a final data validation. This final validation step includes testing for outliers in terms of volume or pattern (e.g. comparison with the 2011 data). When an inconsistency is detected, TESSy data managers or the ESAC-Net coordinator contacts the country for clarification, and where applicable, data are corrected and re-uploaded.
- The data analysis for this 2012 ESAC-Net report is built on TESSy data as of 15 February 2014, followed by a re-upload of 2012 data from three countries between 17 March 2014 and 5 July 2014.

Indicators for reporting antimicrobial consumption

For the community data, two indicators are used to report antimicrobial consumption:

- the number of DDD per 1 000 inhabitants and per day;
- the number of packages per 1 000 inhabitants and per day.

For the hospital sector, and for the few countries for which only total care data (combined reporting of antimicrobial consumption data from the community and the hospital sector) were available, one indicator is used to report antimicrobial consumption:

- the number of DDD per 1 000 inhabitants and per day.

Retrospective changes

Member States can at any time upload or re-upload data to TESSy, e.g. to make corrections.

The following countries re-uploaded data, which may result in differences between data published in this report and data in the 2011 ESAC-Net report:

- Italy: re-uploaded community and hospital sector, antibacterials for systemic use (ATC group J01); antivirals for systemic use (ATC group J05), 2011;
- Latvia: re-uploaded data for the hospital sector for 2011.
- Lithuania: re-uploaded 2010 data as total care data (data had previously been reported separately for the community and the hospital sector);
- Romania: re-uploaded 2011 data as total care data (data had previously been reported separately for the community and the hospital sector).

Additionally, all historical ESAC project data (1997–2009) were re-validated [9] and uploaded to TESSy which resulted in slight differences in the consumption of antibacterials for systemic use (ATC group J01) compared with the 2010 ESAC-Net report where the data (1997–2009) were cited directly from the ESAC project yearbook [10] without verification.

There are two exceptions: the 2002 national reference data from the Czech Republic for the community and similar data for Portugal in 2007 could not be uploaded to TESSy for technical reasons and are therefore not shown (see Tables A1 and A2 in Annex 2).

In addition to ESAC-Net reports, data up to the fourth ATC group level (including all historical data since 1997) are made publically available via the interactive ESAC-Net database [5], where country overview sheets summarising the national results are also provided. The database always shows the latest version of the ESAC-Net data, i.e. includes any data that have been added or re-uploaded by a country after production of the report.

Additionally, Eurostat population data are regularly updated. Retroactive updates can impact the calculated antimicrobial consumption for those countries which use Eurostat data as population data, as they are the denominator for the antimicrobial consumption indicators DDD (or packages) per 1 000 inhabitants and per day.

Therefore, it is possible that data shown in this report may differ slightly from those available from the ESAC-Net interactive database.

EU/EEA consumption

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 and per day of each country with its corresponding Eurostat total population, and then divided by the total EU population.

Trend analysis

National trends in the consumption of antibacterials for systemic use (ATC group J01, including subgroups up to group level 4), and antimycotics and antifungals for systemic use (ATC groups J02 & D01BA) were assessed for the community and the hospital sector over the last five years (2008–2012). A linear regression was applied (p-value considered for statistical significance: <0.05) with the dependent variable being antimicrobial consumption in DDD per 1 000 inhabitants and per day, and the explanatory variable being the year. Countries were excluded if they (a) had one or more years of missing data (Croatia, Romania and Slovakia for community data; Belgium, Hungary, Italy, Lithuania, Luxembourg and Portugal for hospital sector data), (b) reported different types of data (sales or reimbursement) for different years (Hungary, Portugal and Romania for community data), or (c) reported a mixture of community and total care data during the period of analysis (Greece, Iceland and Lithuania for community data; Italy for hospital sector data) (see Chapters 3.1.2–3.1.8, 3.2, 3.3, 4.1 and 4.2).

Map scales

For all maps shown in the report, countries are divided into categories. Countries that did not report any consumption are considered separately from the countries that reported consumption data. The latter are divided into five categories specified as the five equidistant intervals between the minimum (excluding zero) and maximum values for 2012 data. This method displays the countries based on their position in the range of values and better highlights clusters and outliers.

2.4 Data sources

In 2012, data were collated from 28 EU Member States and two EEA countries (Iceland and Norway). The data sources for ESAC-Net are national sales and reimbursement data, including information from national drug registries. Data were collected at the product level for antibacterials for systemic use (ATC group J01), antimycotics and antifungals for systemic use (ATC groups J02 & D01BA), antimycobacterials (ATC group J04), and antivirals for systemic use (ATC group J05). In addition, data on a few other antimicrobials outside of ATC group J were also collected.

Population data from Eurostat, or from national statistical reports, are used for the denominator. When consumption data do not cover the whole population, countries must provide information on the population covered by the reported data.

Table 2.1 provides an overview by country of the healthcare sectors from which the data were provided: data type (origin of data), population coverage, and which of the four different categories of antimicrobial the data were reported for. Twenty-five countries reported data from the community. Twenty of these countries (including Croatia, Lithuania and Slovakia for the first time in ESAC-Net) separately uploaded data from the hospital sector. Cyprus, Iceland and Romania were only able to report data from both sectors combined (total care).

For the community (primary care sector), antimicrobial consumption data were obtained from the Ministry of Health or the national medicines agencies by half of the countries. One third of the countries reported reimbursement data while the remaining countries reported sales data. Two countries reported both sales and reimbursement data. For most countries, the data coverage was reported as being 100%. Germany, Luxembourg, and the Netherlands reported data that covered 80–95% of the population. Most countries provided data on all antimicrobial categories under surveillance by ESAC-Net. Croatia, Ireland, Poland, Spain and the United Kingdom only reported data on antibacterials for systemic use (ATC group J01).

For the hospital sector, 60% of the countries obtained antimicrobial consumption data from the Ministry of Health or national medicines agencies. Ireland, Luxembourg, the Netherlands, Norway and Slovenia obtained data from national hospital networks. Most countries reported sales data, but Belgium, Croatia and Italy only reported reimbursement data, while four countries reported both reimbursement and sales data. The data coverage was 100% with the exception of Ireland, Luxembourg, the Netherlands and Portugal, which reported population coverage between 79 and 95%. All countries, except Croatia, Ireland and the Netherlands, provided data on all categories under surveillance in ESAC-Net.

In 2012, 19 countries (63% of those reporting data for the community) chose the preferred standard option of uploading data to TESSy, with complete national registry data, to provide data for the community or for both healthcare sectors combined (total care). For the hospital sector, 14 countries (70% of those reporting data for the hospital sector) used this standard option to provide data.

Compared with 2011, three countries had changed the type of data reported. Italy reported only sales and not reimbursement data in addition to sales data for the community for 2012. Poland (community) and Romania (total care data) reported sales data instead of reimbursement data in 2012. Croatia reported data separately for the community and the hospital sector for the first time to ESAC-Net. All countries except Poland and Romania, which in 2012 reported data from a market research company instead of data from the Ministry of Health, used the same data providers for 2012 as for 2011 data.

Table 2.1 provides information on the data sources used for denominator data. Thirteen countries provided a data coverage compatible with Eurostat data. This is the preferred approach. These countries did not need to provide national population data to ESAC-Net since TESSy automatically applies Eurostat population data for the calculations. The remaining countries provided their own population data. Luxembourg provided and applied the population covered by health insurance.

Comment

ESAC-Net aims for all network participants to use the ESAC-Net standard option for reporting antimicrobial consumption data (i.e. at the medicinal product level and with a valid national register of available antimicrobials), thus ensuring harmonised reporting of the consumption data in DDD by use of a standardised calculation procedure in TESSy. In addition, the standard option of ESAC-Net allows for a better validation and further analysis of data than the 'light' option (reporting aggregated DDD). For 2012, two thirds of the countries reporting community and hospital sector data, and two out of three countries reporting total care data, used this standard option for reporting ESAC-Net data.

Analyses of antimicrobial consumption trends rely on countries consistently reporting data of the same type and from the same provider. This is the case for most of the countries. Poland and Romania (total care data) reported sales data instead of reimbursement data for the community in 2012 and thus improved reporting as the data now include antimicrobials that may have been dispensed without a prescription and other non-reimbursed courses. Trends for these countries and healthcare sectors should therefore be interpreted with caution. The availability, in four countries, of reimbursement data in addition to sales data allowed for additional quality checks of the data.

Reimbursement data do not include antimicrobials obtained without a prescription and other non-reimbursed courses, and thus underestimate antimicrobial consumption in the community in those countries where over-the-counter dispensation of antimicrobials is known to occur [11]. Where appropriate, this limitation is mentioned in the footnotes of tables and figures in this report.

Table 2.1. Data sources used for surveillance of antimicrobial consumption, by country, 2012

Country	Sector	Consumption							Population data source
		Data provider	Data type	Data Coverage (%) (population under surveillance)	Antibacterials for systemic use (ATC group J01)*	Antimycotics and antifungals for systemic use (ATC groups J02 & D01BA)	Antimycobacterials (ATC group J04)	Antivirals for systemic use (ATC group J05)	
Austria	C	Health insurance company	Reimbursement	100	Y	Y	Y	Y	Eurostat
Belgium	C	Health insurance company	Reimbursement	98	Y	Y	Y	Y	Eurostat
	HC	Health insurance company	Reimbursement	98	Y	Y	Y	Y	Eurostat
Bulgaria	C	Market research company	Sales	100	Y	Y	Y	Y	National Statistics Agency
	HC	Market research company	Sales	100	Y	Y	Y	Y	National Statistics Agency
Croatia	C	Health insurance company	Reimbursement	100	Y	N	N	N	National Statistics Agency
	HC	Ministry of Health	Reimbursement	100	Y	N	N	N	National Statistics Agency
Cyprus	TC	Ministry of Health	Sales	100	Y	Y	Y	Y	Eurostat
Czech Republic	C	Health insurance company	Reimbursement	100	Y	Y	Y	Y	National Statistics Agency
Denmark	C	Ministry of Health	Sales	100	Y	Y	Y	Y	Eurostat
	HC	Ministry of Health	Sales	100	Y	Y	Y	Y	Eurostat
Estonia	C	Medicines Agency	Sales	100	Y	Y	Y	Y	Eurostat
	HC	Medicines Agency	Sales	100	Y	Y	Y	Y	Eurostat
Finland	C	Medicines Agency	Sales	100	Y	Y	Y	Y	Eurostat
	HC	Medicines Agency	Sales	100	Y	Y	Y	Y	Eurostat
France	C	Medicines Agency	Sales	100	Y	Y	Y	Y	National Statistics Agency
	HC	Medicines Agency	Sales	100	Y	Y	Y	Y	National Statistics Agency
Germany	C	Health insurance company	Reimbursement	85	Y	Y	Y	Y	National Statistics Agency
Greece	C	Medicines Agency	Sales	100	Y	Y	Y	Y	Eurostat
	HC	Medicines Agency	Sales	100	Y	Y	Y	Y	Eurostat
Hungary	C	Health insurance company	Reimbursement	100	Y	Y	Y	Y	Eurostat
Iceland	TC	Medicines Agency	Sales	100	Y	Y	Y	Y	National Statistics Agency
Ireland	C	Market research company	Sales	100	Y	N	N	N	Eurostat
	HC	Hospital network	Sales/reimbursement	90	Y	Y	N	N	Eurostat
Italy	C	Medicines Agency	Sales	90	Y	Y	Y	Y	Ministry of Health
	HC	Medicines Agency	Reimbursement	100	Y	Y	Y	Y	Ministry of Health
Latvia	C	Medicines Agency	Sales	100	Y	Y	Y	Y	Eurostat
	HC	Medicines Agency	Sales	100	Y	Y	Y	Y	Eurostat
Lithuania	C	Medicines Agency	Sales	100	Y	Y	Y	Y	Eurostat
	HC	Medicines Agency	Sales	100	Y	Y	Y	Y	Eurostat
Luxembourg	C	Health insurance company	Reimbursement	94	Y	Y	Y	Y	Health insurance company
	HC	Hospital network	Sales	90	Y	Y	Y	Y	National Statistics Agency
Malta	C	Ministry of Health	Sales	100	Y	Y	Y	Y	Ministry of Health
	HC	Ministry of Health	Sales	100	Y	Y	Y	Y	Ministry of Health
Netherlands	C	Community pharmacists	Sales	92	Y	Y	Y	Y	Other
	HC	Hospital network	Sales	79	Y	N	N	N	National Statistics Agency
Norway	C	Other	Sales/reimbursement	100	Y	Y	Y	Y	National Statistics Agency
	HC	Hospital network	Sales/reimbursement	100	Y	Y	Y	Y	Other
Poland	C	Market research company	Sales	100	Y	N	N	N	Eurostat
Portugal	C	Ministry of Health	Sales	100	Y	Y	Y	Y	Ministry of Health
	HC	Ministry of Health	Sales/reimbursement	95	Y	Y	Y	Y	Ministry of Health
Romania	TC	Market research company	Sales	100	Y	Y	N	Y	National Statistics Agency
Slovakia	C	Medicines Agency	Sales	100	Y	Y	Y	N	Eurostat
	HC	Medicines Agency	Sales	100	Y	Y	Y	N	Eurostat
Slovenia	C	Other	Sales/reimbursement	100	Y	Y	Y	Y	National Statistics Agency
	HC	Hospital network	Sales/reimbursement	100	Y	Y	Y	Y	National Statistics Agency
Spain	C	Ministry of Health	Reimbursement	100	Y	N	N	N	National Statistics Agency
Sweden	C	Community pharmacists	Sales	100	Y	Y	Y	Y	National Statistics Agency
	HC	Other	Sales	100	Y	Y	Y	Y	National Statistics Agency
United Kingdom	C	Ministry of Health	Reimbursement	100	Y	N	N	N	National Statistics Agency

** Oral and rectal nitroimidazole derivates as antiprotozoals (ATC subgroup P01AB), oral vancomycin as intestinal anti-infective (ATC chemical substance A07AA09) are reported, but data are not presented in this report.*
C: community; HC: hospital care; TC: total care; Y: yes; N: no.

3 Consumption of antimicrobials for systemic use in the community

This chapter covers data on consumption of antibacterials and of antimycotics and antifungals for systemic use in the community (i.e. outside hospitals).

3.1 Consumption of antibacterials for systemic use (ATC group J01)

3.1.1 Defined daily doses and number of packages per 1 000 inhabitants and per day

Results for the indicator 'DDD per 1 000 inhabitants and per day'

All 30 countries participating in ESAC-Net reported data on consumption of antibacterials for systemic use (ATC group J01) in the community for 2012. As in previous years, there were large inter-country variations in consumption. These variations were observed both for the total consumption of antibacterials for systemic use (ATC group J01) and for all subgroups of antibacterials for systemic use, i.e. at ATC group level 3.

Results for Cyprus, Iceland and Romania which reported total care data in 2012, are shown jointly with the consumption data for the community (primary care sector).

The total consumption of antibacterials for systemic use (ATC group J01) in the community ranged from 11.3 DDD per 1 000 inhabitants and per day (the Netherlands) to 31.9 DDD per 1 000 inhabitants and per day (Greece). The population-weighted EU/EEA mean consumption was 21.5 DDD per 1 000 inhabitants and per day.

Figure 3.2 shows a north–south gradient with the lowest consumption (<19.6 DDD per 1 000 inhabitants and per day) in the north of Europe, e.g. Scandinavian and Baltic countries, and the highest consumption (≥19.6 DDD per 1 000 inhabitants and per day) in the south of Europe, e.g. Greece and Romania.

Between 2011 and 2012, consumption decreased by more than 1% in 15 (56%) of 27 countries reporting for the same sector in both years (Austria, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, Greece, Hungary, Italy, Malta, Poland, Portugal, Romania, Sweden). During the same period, consumption increased by more than 1% in seven (26%) of 27 countries (Belgium, France, Germany, Ireland, Latvia, Norway and the United Kingdom). Five countries (Iceland, Luxembourg, the Netherlands, Slovenia and Spain) only showed a difference in consumption of antibacterials for systemic use (ATC group J01) of less than 1% between 2011 and 2012 (Table 3.3).

Lithuania and Slovakia reported consumption data as total care data in 2011 and separately for the community and the hospital sector in 2012, which means that the trends could not be measured because of the change in the type of data provided. Since 1997, the number of reporting EU/EEA countries increased substantially from 14 countries in 1997 to 30 countries in 2012. Table A1 of Annex 2 provides an overview, by country, for the period 1997–2012.

Consumption of seven major subgroups of antibacterials for systemic use (ATC group J01) in the community in 2012 is presented in Table 3.1 and in Figure 3.1. Results for the subgroups are presented in detail in Chapters 3.1.2–3.1.8.

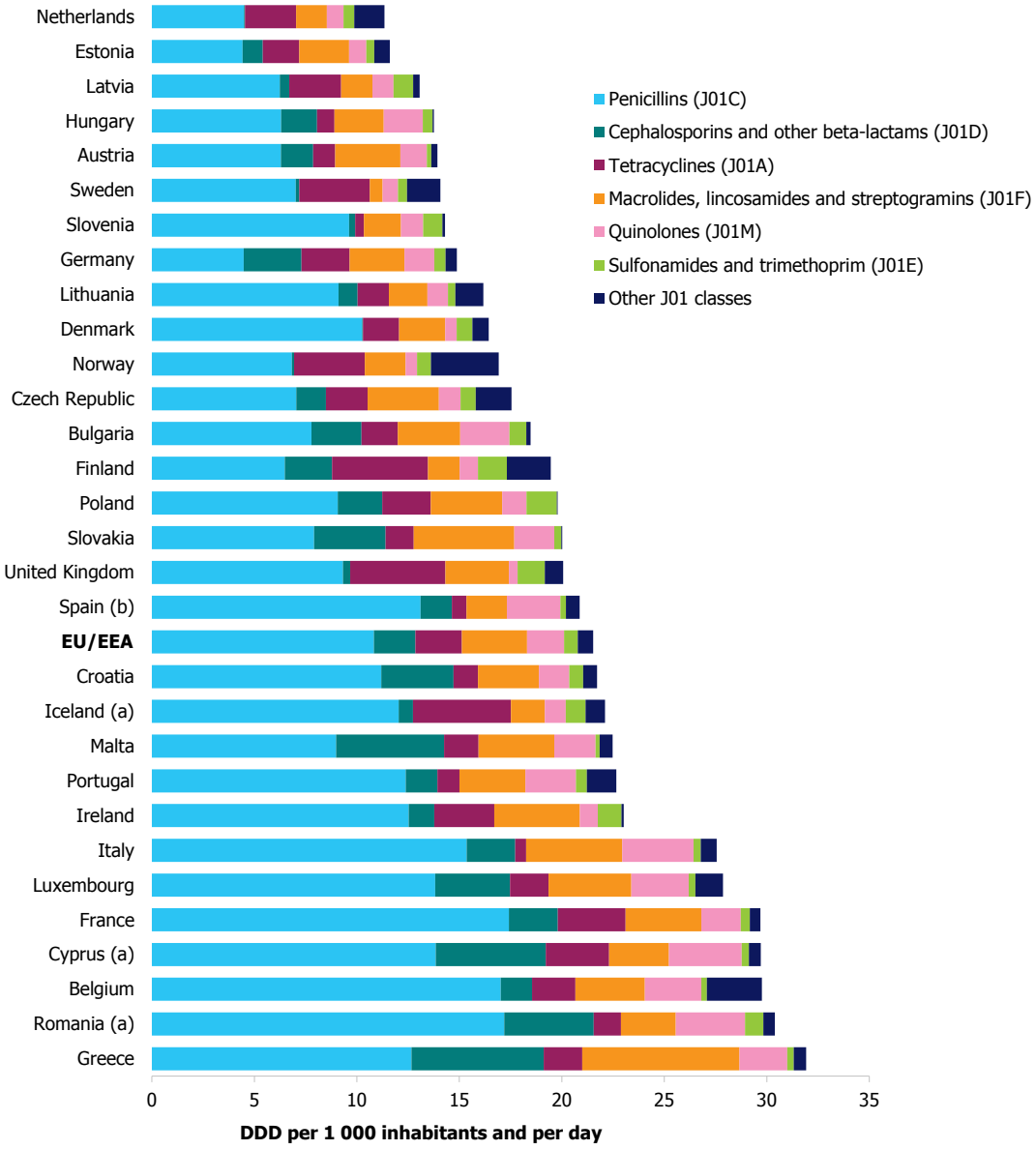
In 2012, more than 50% of the consumption of antibacterials for systemic use (ATC group J01) in the community was made up of 12 different antibacterial agents (doxycycline (J01AA02), lymecycline (J01AA04), amoxicillin (J01CA04), pivmecillinam (J01CA08), phenoxymethylpenicillin (J01CE02), benzathine phenoxymethylpenicillin (J01CE10), flucloxacillin (J01CF05), amoxicillin and enzyme inhibitor (J01CR02), cephalexin (J01DB01), cefuroxime (J01DC02), clarithromycin (J01FA09), azithromycin (J01FA10) and methenamine (J01XX05). Of these agents, six are penicillins (ATC group J01C). In 22 (73%) of the 30 EU/EEA countries, three or fewer different agents were responsible for more than 50% of the consumption of antibacterials for systemic use (ATC group J01). Amoxicillin, alone (ATC code J01CA04) or in combination with an enzyme inhibitor (J01CR02), was the antibacterial agent most often consumed in these 22 countries, with the exception of Norway and Sweden where the most consumed agent was phenoxymethylpenicillin (J01CE02).

Table 3.1. Consumption of antibacterials for systemic use (ATC group J01) at ATC group level 3 in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day

Country	Tetra-cyclines (J01A)	Beta-lactams, penicillins (J01C)	Other beta-lactam antibac-terials (J01D)	Sulfonamides and trimethoprim (J01E)	Macrolides, lincosamides and strepto-gramins (J01F)	Quino-lones (J01M)	Other antibac-terials (J01X)	Sum (J01B, J01G, and J01R)*	Total (ATC group J01)
Austria	1.1	6.3	1.6	0.2	3.2	1.3	0.3	<0.1	13.9
Belgium	2.1	17.0	1.5	0.3	3.4	2.8	2.6	<0.1	29.8
Bulgaria	1.8	7.8	2.4	0.8	3.0	2.4	<0.1	0.2	18.5
Croatia	1.2	11.2	3.5	0.7	3.0	1.5	0.7	0.0	21.7
Cyprus (a)	3.1	13.8	5.4	0.4	2.9	3.5	0.5	0.1	29.7
Czech Republic	2.0	7.0	1.4	0.7	3.5	1.1	1.2	0.6	17.5
Denmark	1.8	10.3	0.0	0.8	2.3	0.6	0.8	<0.1	16.4
Estonia	1.8	4.4	1.0	0.4	2.4	0.8	0.8	<0.1	11.6
Finland	4.7	6.5	2.3	1.4	1.6	0.9	2.1	<0.1	19.5
France	3.3	17.4	2.4	0.4	3.7	1.9	0.5	<0.1	29.7
Germany	2.3	4.5	2.8	0.6	2.7	1.4	0.5	<0.1	14.9
Greece	1.9	12.7	6.5	0.3	7.7	2.3	0.5	0.1	31.9
Hungary	0.9	6.3	1.8	0.5	2.4	1.9	<0.1	<0.1	13.8
Iceland (a)	4.8	12.0	0.7	1.0	1.7	1.0	0.9	<0.1	22.1
Ireland	2.9	12.5	1.2	1.2	4.2	0.9	0.1	<0.1	23.0
Italy	0.5	15.4	2.4	0.4	4.7	3.5	0.7	0.1	27.6
Latvia	2.5	6.2	0.5	1.0	1.5	1.0	0.3	0.1	13.1
Lithuania	1.5	9.1	0.9	0.4	1.9	1.0	1.3	<0.1	16.2
Luxembourg	1.9	13.8	3.6	0.3	4.0	2.8	1.3	<0.1	27.9
Malta	1.7	9.0	5.3	0.2	3.7	2.0	0.3	0.3	22.5
Netherlands	2.5	4.5	0.0	0.5	1.5	0.8	1.4	<0.1	11.3
Norway	3.4	6.8	0.1	0.7	2.0	0.6	3.3	<0.1	16.9
Poland	2.4	9.1	2.2	1.5	3.5	1.2	<0.1	<0.1	19.8
Portugal	1.1	12.4	1.5	0.5	3.2	2.5	1.4	<0.1	22.7
Romania (a)	1.3	17.2	4.4	0.9	2.7	3.4	0.1	0.4	30.4
Slovakia	1.4	7.9	3.5	0.3	4.9	2.0	<0.1	<0.1	20.0
Slovenia	0.4	9.6	0.3	0.9	1.8	1.1	0.1	<0.1	14.3
Spain (b)	0.7	13.1	1.5	0.3	2.0	2.6	0.4	0.2	20.9
Sweden	3.4	7.0	0.2	0.4	0.6	0.7	1.6	<0.1	14.1
United Kingdom	4.6	9.3	0.4	1.3	3.1	0.4	0.9	<0.1	20.1
EU/EEA mean (population-weighted)	**2.3**	**10.8**	**2.0**	**0.7**	**3.2**	**1.8**	**0.7**	**0.1**	**21.5**

(a) Cyprus, Iceland 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*

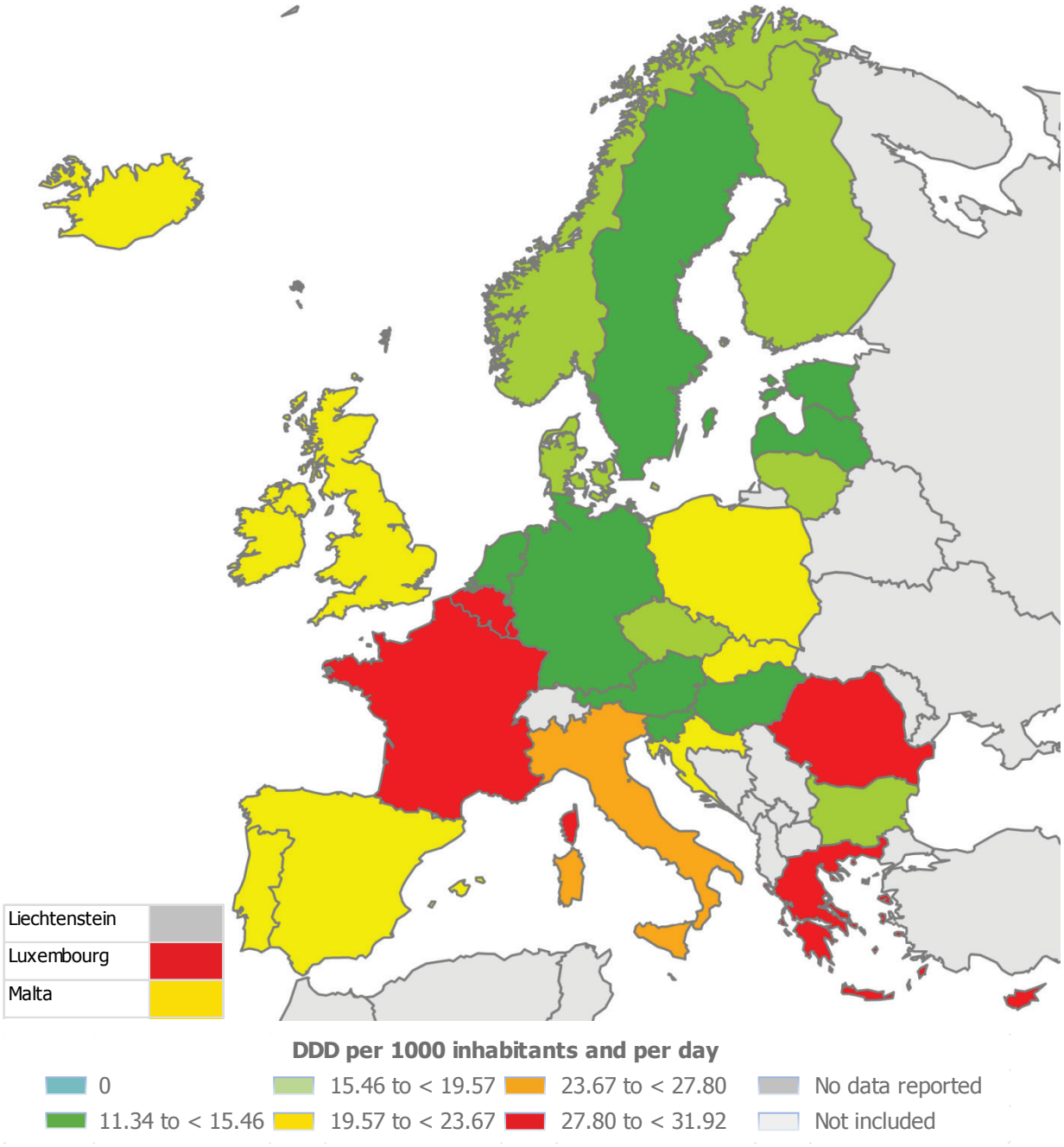
Figure 3.1. Consumption of antibacterials for systemic use (ATC group J01) at ATC group level 3 in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day



(a) Cyprus, Iceland 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.

Consumption of amphenicols (ATC group J01B), aminoglycosides (ATC group J01G) and combinations of antibacterials (ATC group J01R) are presented together in Table 3.1, but are included with other antibacterials (ATC group J0X) as 'other J01 classes' in Figure 3.1. In 2012, consumption of these three ATC groups (J01B, J01G and J01R) in the community varied from 0.002 DDD per 1 000 inhabitants and per day (Portugal) to 0.6 DDD per 1 000 inhabitants and per day (Czech Republic). Croatia did not report any consumption of this group.

Figure 3.2. Consumption of antibacterials for systemic use (ATC group J01) in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day



Cyprus, Iceland 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.
For more information on the map scales, see Chapter 2.3.

Results for the indicator 'number of packages per 1 000 inhabitants and per day'

In 2012, 21 countries reported data on the number of consumed packages of antibacterials for oral use (Table 3.2. and Figure 3.3). The total consumption of antibacterials for systemic use (ATC group J01, oral administration) in the community ranged from 1.1 packages per 1 000 inhabitants and per day (Sweden) to 4.9 packages per 1 000 inhabitants and per day (France). On average, 3.1 packages of antibacterials for systemic use (ATC group J01) were consumed per 1 000 inhabitants and per day in EU/EEA countries in 2012.

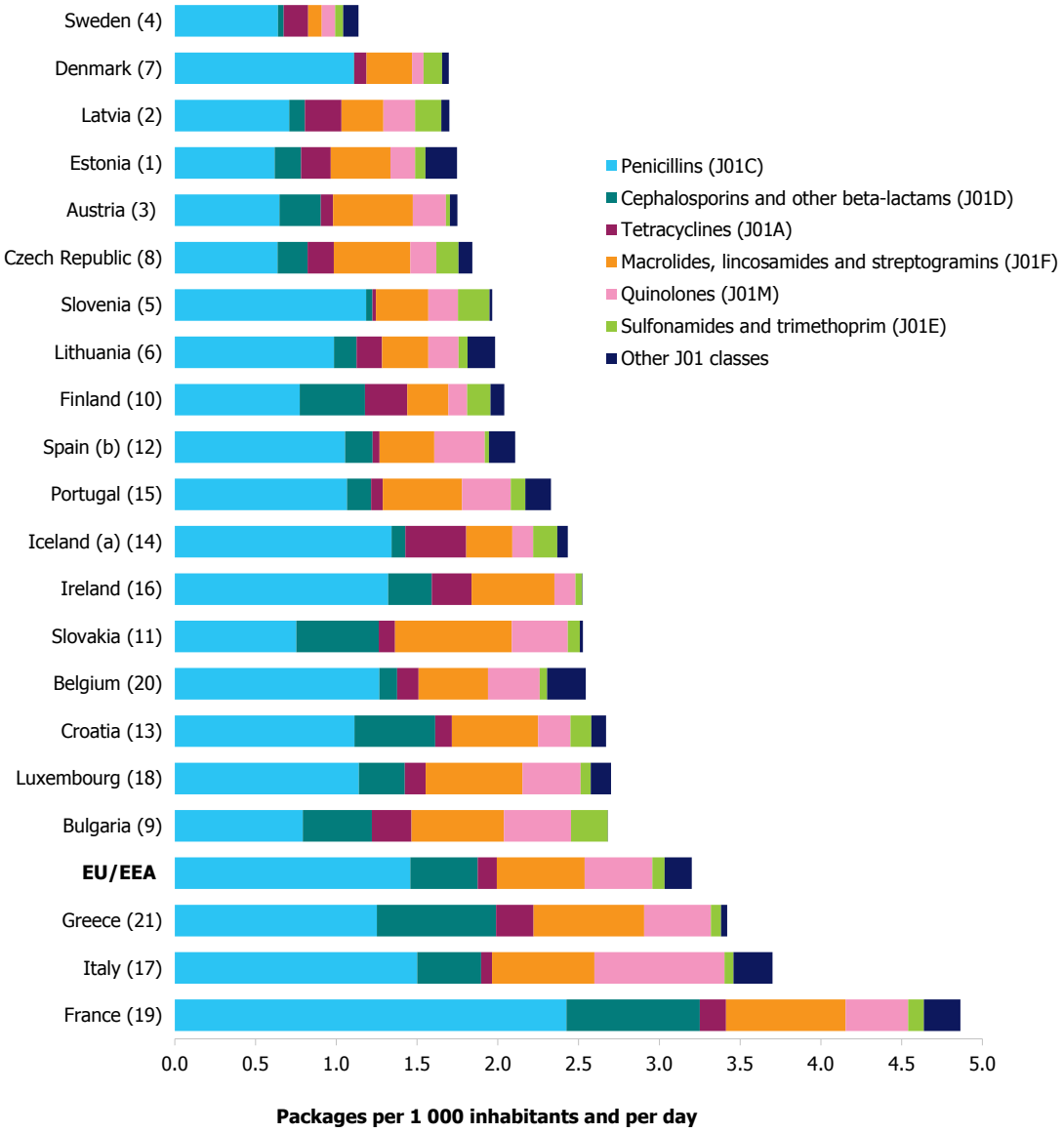
When considering major ATC groups, average consumption ranged from 0.07 packages per 1 000 inhabitants and per day for sulfonamides and trimethoprim (ATC group J01E) to 1.4 packages per 1 000 inhabitants and per day for penicillins (ATC group J01C).

Table 3.2. Consumption of packages of antibacterials for systemic use (ATC group J01, oral administration) in the community, EU/EEA countries, 2012, expressed as packages per 1 000 inhabitants and per day

Country	Tetra-cyclines (J01A)	Beta-lactams, penicillins (J01C)	Other beta-lactam antibacterials (J01D)	Sulfonamides and trimethoprim (J01E)	Macrolides, lincosamides and strepto-gramins (J01F)	Quino-lones (J01M)	Other antibacterials (J01X)	Sum (J01B, J01G, and J01R)*	Total (ATC group J01)
Austria	0.08	0.65	0.26	0.03	0.49	0.20	0.05	0	1.75
Belgium	0.13	1.27	0.11	0.05	0.43	0.32	0.24	0	2.54
Bulgaria	0.24	0.79	0.43	0.23	0.57	0.42	0.00	0.09	2.78
Croatia	0.1	1.11	0.5	0.13	0.53	0.2	0.09	0	2.67
Czech Republic	0.16	0.64	0.19	0.14	0.47	0.16	0.09	0	1.84
Denmark	0.08	1.11	0.00	0.12	0.28	0.07	0.04	0	1.70
Estonia	0.18	0.62	0.16	0.06	0.37	0.15	0.20	0	1.75
Finland	0.26	0.77	0.40	0.14	0.25	0.12	0.08	0	2.04
France	0.16	2.42	0.83	0.10	0.74	0.39	0.23	<0.01	4.86
Greece	0.23	1.25	0.74	0.06	0.68	0.41	0.04	0	3.42
Iceland (a)	0.38	1.34	0.09	0.15	0.29	0.13	0.07	0	2.43
Ireland	0.25	1.32	0.27	0.04	0.51	0.13	0.00	<0.01	2.52
Italy	0.07	1.50	0.40	0.06	0.63	0.81	0.24	0	3.70
Latvia	0.23	0.71	0.10	0.16	0.26	0.20	0.05	0	1.70
Lithuania	0.16	0.99	0.14	0.06	0.29	0.19	0.17	0	1.98
Luxembourg	0.13	1.14	0.28	0.06	0.60	0.36	0.13	0	2.70
Portugal	0.07	1.07	0.15	0.09	0.49	0.30	0.16	0	2.33
Slovakia	0.10	0.75	0.51	0.07	0.72	0.35	0.02	<0.01	2.53
Slovenia	0.02	1.18	0.04	0.20	0.32	0.18	0.02	0	1.96
Spain (b)	0.04	1.05	0.17	0.03	0.34	0.31	0.16	0.03	2.14
Sweden	0.15	0.64	0.04	0.05	0.08	0.08	0.09	0	1.14
EU/EEA mean (population-weighted)	**0.12**	**1.40**	**0.42**	**0.07**	**0.55**	**0.41**	**0.16**	**0.01**	**3.13**

(a) Iceland 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 based on the 21 countries that provided data.
**J01B: amphenicols; J01G: aminoglycoside antibacterials; J01R: combinations of antibacterials*

Figure 3.3. Consumption of packages of antibacterials for systemic use (ATC group J01, oral administration) in the community in EU/EEA countries, 2012, at group level 3, expressed as packages per 1 000 inhabitants and per day



(a) Iceland 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.
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 and per day (see Figure 3.1).
EU/EEA refers to the corresponding population-weighted mean consumption based on the 21 countries that provided data.

Trends for the indicator 'DDD per 1 000 inhabitants and per day'

Trends in the community consumption of antibacterials for systemic use (ATC group J01) expressed in DDD per 1 000 inhabitants and per day for the period 2008–2012 are presented in Table 3.3 (see also Chapter 2.3 for trend analyses).

A significant increasing trend in the consumption of antibacterials for systemic use (ATC group J01) during 2008–2012 was observed for only five countries (Belgium, Latvia, Norway, Spain and the United Kingdom). Austria showed a significant decreasing trend in the consumption of antibacterials for systemic use (ATC group J01) during this period.

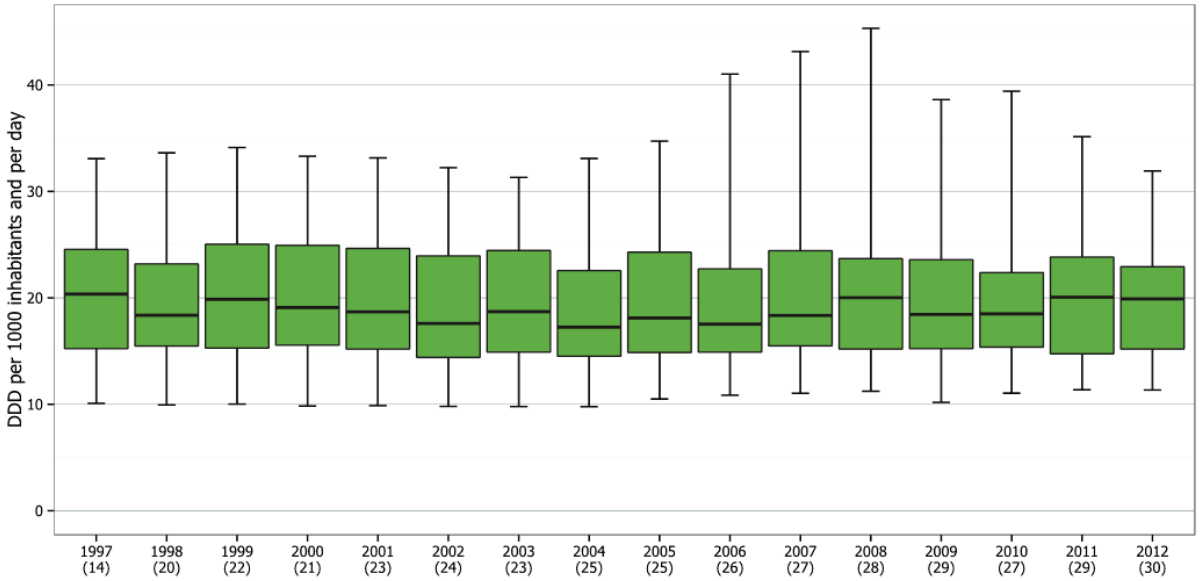
Table 3.3. Trends of consumption of antibacterials for systemic use (ATC group J01) in the community, EU/EEA countries, 2008–2012, expressed as DDD per 1 000 inhabitants and per day

Country	2008	2009	2010	2011	2012	Trends in antimicrobial consumption, 2008–2012	Average annual change 2008–2012	Statistical significance
Netherlands	11.2	11.4	11.2	11.4	11.3		0.02	n.s.
Estonia	11.9	11.1	11.1	12.1	11.6		0.04	n.s.
Latvia	11.4	10.9	11.8	12.8	13.1		0.53	significant
Hungary (c)	15.2	16.0	15.7	14.7	13.8			n.a.
Austria	15.1	15.9	15.0	14.5	13.9		-0.34	significant
Sweden	14.6	13.9	14.2	14.3	14.1		-0.09	n.s.
Slovenia	15.0	14.4	14.4	14.4	14.3		-0.12	n.s.
Germany	14.5	14.9	14.5	14.1	14.9		-0.02	n.s.
Lithuania	25.1*	19.5*	17.7*	19.0*	16.2			n.a.
Denmark	16.0	16.0	16.5	17.4	16.4		0.35	n.s.
Norway	15.5	15.2	15.8	16.5	16.9		0.40	significant
Czech Republic	17.4	18.4	17.9	18.5	17.5		0.02	n.s.
Bulgaria	20.6	18.6	18.2	19.5	18.5		-0.25	n.s.
Finland	18.3	18.0	18.5	20.1	19.5		0.55	n.s.
Poland (c)	20.7	23.6	21.0	21.9	19.8			n.a.
Slovakia (a)	23.4	23.8		23.8*	20.0			n.a.
United Kingdom	16.9	17.3	18.7	18.8	20.1		0.76	significant
Spain (b)	19.7	19.7	20.3	20.9	20.9		0.34	significant
EU/EEA	**21.0**	**20.9**	**20.9**	**21.5**	**21.5**		**0.18**	**n.s.**
Croatia (a)					21.7			n.a.
Iceland	20.6	19.4	22.3*	22.3*	22.1*			n.a.
Malta	20.8	21.6	21.3	23.4	22.5		0.51	n.s.
Portugal	22.6	22.9	22.4	23.2	22.7		0.02	n.s.
Ireland	22.4	20.8	20.3	22.6	23.0		0.30	n.s.
Italy	28.5	28.7	27.3	28.2	27.6		-0.22	n.s.
Luxembourg	27.1	28.2	28.6	27.6	27.9		0.09	n.s.
France	28.0	29.6	28.2	28.7	29.7		0.24	n.s.
Cyprus	32.8*	34.4*	31.0*	32.0*	29.7*		-0.88	n.s.
Belgium	27.7	27.5	28.4	29.0	29.8		0.55	significant
Romania (a)(b)(c)		10.2		30.9*	30.4*			n.a.
Greece	45.2*	38.6	39.4*	35.1	31.9			n.a.

**Total care data, including the hospital sector.*
(a) Croatia (2008–2011), Romania (2008 and 2010) and Slovakia (2010) did not report data for these years.
(b) Spain (2008–2012) and Romania (2009) reported reimbursement data, i.e. not including consumption without a prescription and other non-reimbursed courses.
(c) Hungary, Poland and Romania changed the type of data reported between 2008 and 2012 (reimbursement versus sales data).
EU/EEA refers to the corresponding population-weighted mean consumption.
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 2008 and 2012.
n.s.: not significant.

Overall trends in the annual EU/EEA median consumption for the EU/EEA countries that reported data to the ESAC project and ESAC-Net for the year 1997 and onwards are shown in boxplot figures for the corresponding ATC groups. Between 2011 and 2012 no increasing or decreasing trend was observed (Figure 3.4). The EU/EEA population-weighted mean consumption of antibacterials for systemic use did not change significantly between 2008 and 2012.

Figure 3.4. Trends and inter-country variations of antibacterials for systemic use (ATC group J01) in the community, EU/EEA countries, 1997–2012, expressed as DDD per 1 000 inhabitants and per day



Boxes indicate the lower and the upper quartiles. The bold lines indicate the medians. Whiskers indicate the minimum and maximum values. For 1997–2009, only data from ESAC participating countries that also participated in ESAC-Net in 2012 are included. The number of participating countries is shown in parentheses.

Discussion

In 2012, the EU/EEA population-weighted mean consumption of antibacterials for systemic use (ATC group J01) was at the same level as in 2011 and did not significantly change during the period 2008–2012, whereas a general decrease had previously been observed during 1999–2004 followed by a gradual increase between 2004 and 2008 [10].

Two countries (Greece and Poland) that reported data for the same sectors for both years, showed a remarkable decrease of more than 9% in consumption between 2011 and 2012. Greece started a campaign on prudent use of antibiotics in 2008 and continued with annual seminars for primary care doctors and issued corresponding guidelines for antibiotic use. Since 2009, consumption of antibacterials for systemic use (ATC J01) has decreased in Greece. The decrease between 2011 and 2012 coincided with the introduction of an electronic system for prescription of medicines in the community in the last quarter of 2010. The extent to which this new prescription system or other factors such as the economic crisis contributed to the decrease in consumption between 2011 and 2012 has not been evaluated. In Poland, a short-term policy of the National Health Fund to only reimburse prescriptions that followed specific requirements (e.g. microbiological results available, prescribed according to the summary of product characteristics of a medicine as provided by the supplier) resulted in an increase of prescriptions without reimbursement and for which the entire cost of antibacterials was paid by patients. In 2012, Poland changed data provider for reporting to ESAC-Net and reported sales data from the market research company IMS Health (instead of reimbursement data in 2011). As for Greece, the extent to which factors such as the economic crisis or the enforced monitoring of physicians' prescribing behaviour may have led to a stricter adherence to guidelines resulting in a decrease in consumption has not been evaluated.

Short-term decreases or increases in the consumption of antibacterials for systemic use (ATC group J01) were reported in other EU/EEA countries. More information may be provided by these countries in the comments of the country overview sheets available via the ESAC-Net interactive database on the ECDC website [5].

In Lithuania and Slovakia, the apparently large decreases in consumption (-2.8 and -3.8 DDD per 1 000 inhabitants and per day, respectively) observed between 2011 and 2012 are explained by the fact that both countries reported total care data for 2011 and separately for both sectors in 2012 (see Chapter 4.1). For these two countries, antimicrobial consumption data in 2011 and 2012 as reported to ESAC-Net are therefore not comparable.

Antimicrobial consumption expressed in DDD per 1 000 inhabitants and per day cannot directly be extrapolated to a number of prescriptions per patient. Therefore, the indicator 'DDD per 1 000 per inhabitants and per day' may not be sufficient to describe the prescription of antimicrobials in EU/EEA countries.

The ESAC project proposed that the number of consumed packages be used as a proxy for the number of prescription or treatments. A recent study in Belgium showed that for countries dispensing complete packages and with an increasing size of packages (number of DDD per package) over time, antimicrobial consumption expressed as packages per 1 000 inhabitants per day may be a more appropriate measure to assess trends in antibiotic prescribing as well as the impact of awareness campaigns [4].

Starting with the ESAC-Net report 2010, the number of DDD per package was analysed to validate packages as a proxy for prescription. The average number of DDD per package was calculated for the three main ATC groups under surveillance: antibacterials for systemic use (ATC group J01), antimycotics and antifungals for systemic use (ATC groups J02 & D01BA) and antivirals for systemic use (ATC group J05) and stratified by routes of administration and healthcare sectors. It was concluded that, for the community, the number of packages of antibacterials for systemic use (ATC group J01, oral administration) may be an acceptable surrogate for prescriptions of these medicines.

For the first time, antimicrobial community consumption data are jointly presented in this chapter for the two indicators 'DDD per 1 000 inhabitants and per day' and 'packages per 1 000 inhabitants and per day' (Figures 3.1 and 3.3, Tables 3.3 and 3.4; see also Chapter 2.3).

Compared with the ranking of antimicrobial consumption expressed as DDD per 1 000 inhabitants, no country retained the same ranking when the results were expressed as packages per 1 000 inhabitants and per day. A few countries showed an increase (Bulgaria) or decrease (Belgium, Denmark and Portugal) of their ranking position by more than three places when consumption was expressed in packages instead of DDD.

Antibacterials for systemic use (ATC group J01) are often used to treat acute infections. In 2012, an average 3.1 packages of antibacterials for systemic use (ATC group J01) per 1 000 inhabitants and per day were consumed in the 21 countries that reported data on packages. Should further information become available on the average duration of treatments and the actual daily doses used, it would be possible to extrapolate the number of DDDs to a number of prescriptions and treatments.

3.1.2 Tetracyclines (ATC group J01A)

Results

In 2012, consumption of tetracyclines (ATC group J01A) in the community ranged from 0.4 DDD per 1 000 inhabitants and per day (Slovenia) to 4.8 DDD per 1 000 inhabitants and per day (Iceland), with an EU/EEA population-weighted mean of 2.3 DDD per 1 000 inhabitants and per day (Table 3.1). Tetracycline consumption was generally lower in southern Europe than in northern and western Europe (Figure 3.5). Tetracycline consumption as a proportion of the total consumption of ATC group J01 ranged from less than 1.9% (Italy) to 24.4% (Sweden).

The most consumed of all tetracyclines in the community in 2012 was doxycycline which, on average, accounted for 77% of the consumption of this group, followed by lymecycline, minocycline and tetracycline. This pattern is similar to that observed since 2009.

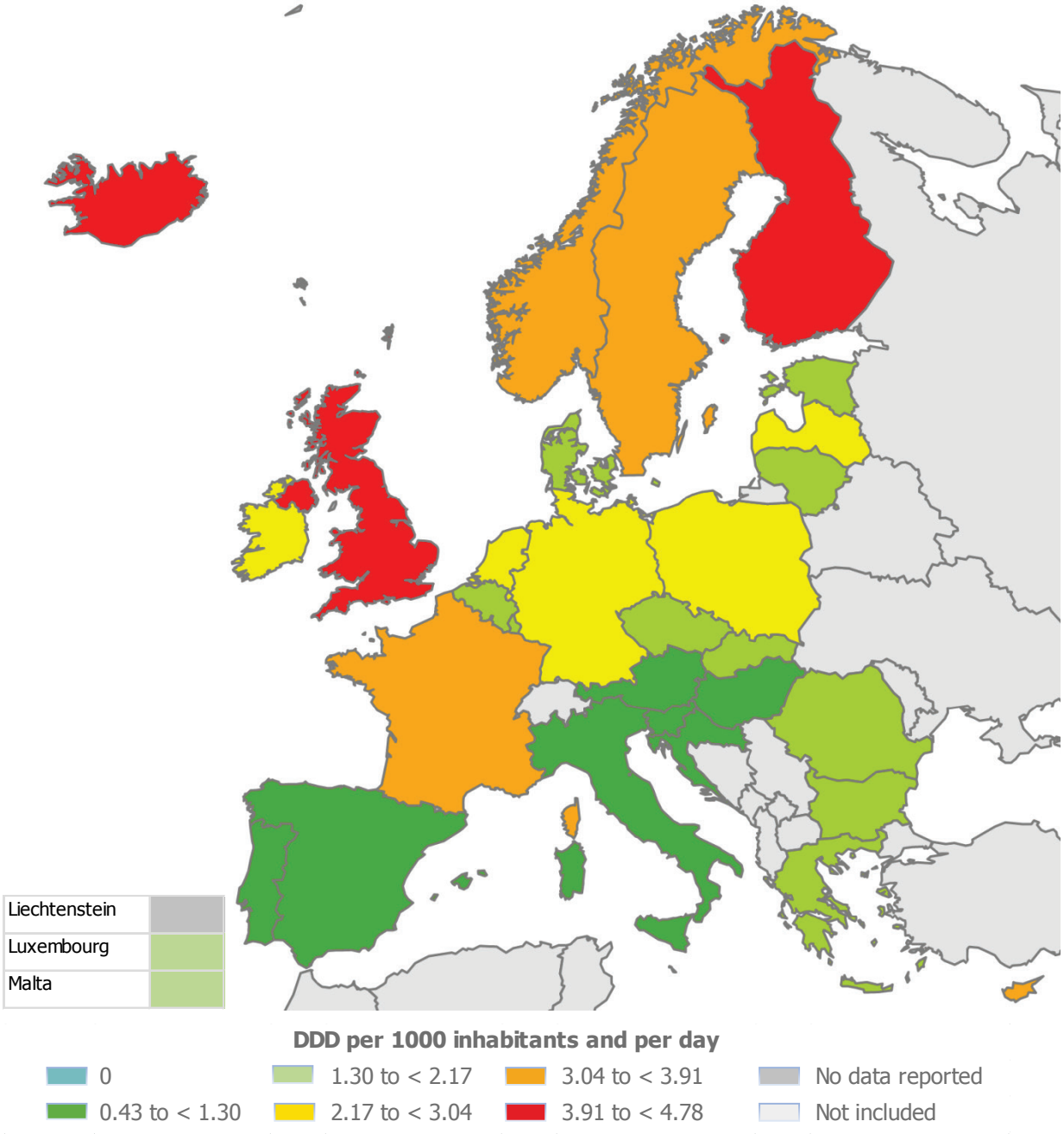
Doxycycline consumption accounted for more than 50% of the total consumption of tetracyclines in 2012 except in Belgium, Denmark, Ireland, Malta and the United Kingdom in 2012. However, some countries have shown a different pattern of consumption of the various tetracyclines since 2009. In 2012, lymecycline was the most frequently consumed of all tetracyclines in the United Kingdom, making up 35.1%, while consumption of doxycycline accounted for only 34.3%.

Trends

Trends in the consumption of tetracyclines (ATC J01A) in the community per country between 2008 and 2012 are shown in Table 3.4. A significant increase in the consumption of tetracyclines (ATC group J01A) was observed for Denmark, Finland, Spain and the United Kingdom over the five-year period 2008–2012. Austria, the Czech Republic, Germany and Luxembourg showed a significant decrease in consumption of tetracyclines (ATC group J01A) during the same period.

The trends in the consumption of tetracyclines (ATC group J01A) in the community are shown in Figure 3.6 and indicate a significant decrease between 1997 and 2009. The EU/EEA population-weighted mean consumption of tetracyclines in the community was 2.3 DDD per 1 000 inhabitants and per day in 2012 and has remained stable since 2008.

Figure 3.5. Consumption of tetracyclines (ATC group J01A) in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day



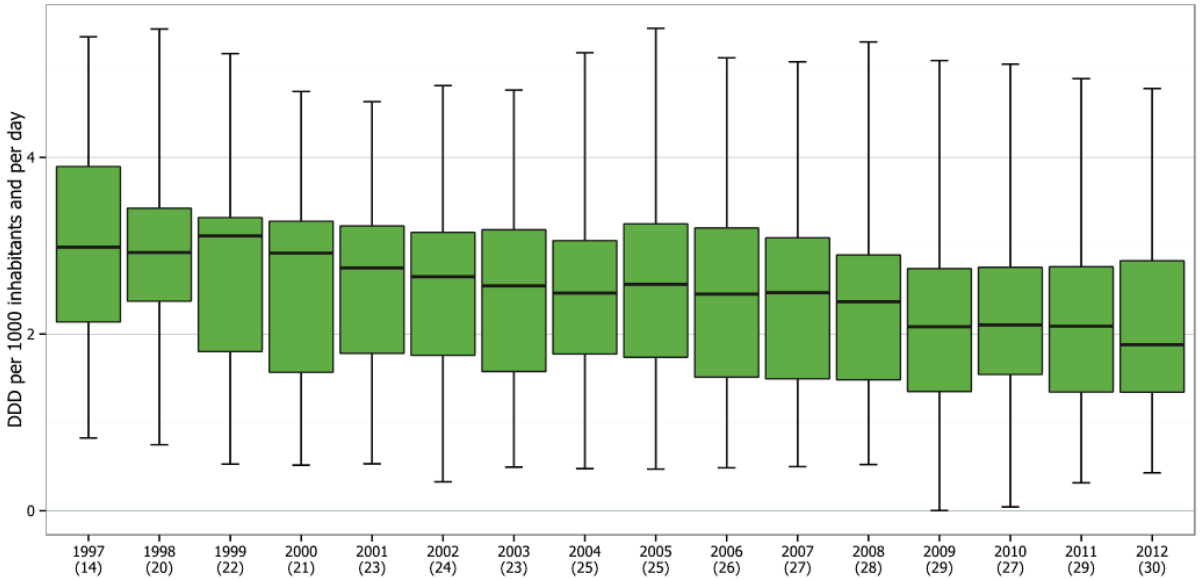
Cyprus, Iceland and Romania provided total care data, i.e. including the hospital sector.
Spain provided reimbursement data, i.e. not including consumption without a prescription and other non-reimbursed courses.
For more information on the map scales, see Chapter2.3.

Table 3.4. Trends of consumption of tetracyclines (ATC group J0A) in the community, EU/EEA countries, 2008–2012, expressed as DDD per 1 000 inhabitants and per day

Country	2008	2009	2010	2011	2012	Trends in antimicrobial consumption, 2008–2012	Average annual change 2008–2012	Statistical significance
Slovenia	0.5	<0.1	<0.1	0.3	0.4		0.01	n.s.
Italy	0.5	0.5	0.5	0.5	0.5		<0.01	n.s.
Spain (b)	0.6	0.6	0.7	0.7	0.7		0.03	significant
Hungary (c)	1.4	1.3	1.4	0.9	0.9			n.a.
Austria	1.3	1.3	1.2	1.2	1.1		-0.06	significant
Portugal	0.8	0.7	0.7	1.0	1.1		0.08	n. s.
Croatia (a)					1.2			n.a.
Romania (a)(b)(c)		0.1		1.3*	1.3*			n.a.
Slovakia (a)	1.5	1.5		1.5*	1.4			n.a.
Lithuania	2.4*	2.0*	1.7*	1.6*	1.5			n.a.
Malta	1.1	1.1	1.0	1.1	1.7		0.11	n.s.
Denmark	1.6	1.6	1.7	1.7	1.8		0.05	significant
Bulgaria	2.2	1.6	1.7	1.8	1.8		-0.06	n.s.
Estonia	2.2	2.1	1.9	2.1	1.8		-0.08	n.s.
Greece	2.4*	2.0	2.3*	2.4	1.9			n.a.
Luxembourg	2.2	2.1	2.0	1.9	1.9		-0.07	significant
Czech Republic	2.5	2.4	2.3	2.2	2.0		-0.12	significant
Belgium	2.2	2.1	2.1	2.1	2.1		-0.02	n.s.
EU/EEA	**2.4**	**2.3**	**2.3**	**2.2**	**2.3**		**-0.29**	**n. s.**
Germany	3.2	3.1	2.7	2.6	2.3		-0.22	significant
Poland (c)	2.5	2.5	2.1	2.0	2.4			n.a.
Netherlands	2.6	2.7	2.7	2.6	2.5		-0.04	n.s.
Latvia	2.4	2.2	2.4	2.5	2.5		0.07	n.s.
Ireland	3.2	2.7	2.6	2.8	2.9		-0.05	n.s.
Cyprus	2.7*	2.9*	3.3*	2.8*	3.1*		0.06	n.s.
France	3.4	3.4	3.2	3.1	3.3		-0.06	n.s.
Sweden	3.2	3.0	3.3	3.5	3.4		0.09	n.s.
Norway	2.8	2.7	2.8	3.1	3.4		0.17	n. s.
United Kingdom	3.7	4.0	4.1	4.3	4.6		0.22	significant
Finland	4.0	4.0	4.1	4.7	4.7		0.21	significant
Iceland	5.3	5.1	5.1*	4.9*	4.8*			n.a.

**Total care data, including the hospital sector.*
(a) Croatia (2008–2011), Romania (2008 and 2010) and Slovakia (2010) did not report data for these years.
(b) Spain (2008–2012) and Romania (2009) reported reimbursement data, i.e. not including consumption without a prescription and other non-reimbursed courses.
(c) Hungary, Poland and Romania changed the type of data reported between 2008 and 2012 (reimbursement versus sales data).
EU/EEA refers to the corresponding population-weighted mean consumption.
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 2008 and 2012.
n.s.: not significant.

Figure 3.6. Trends and inter-country variations of consumption of tetracyclines (ATC group J01A) in the community, EU/EEA countries, 1997–2012, expressed as DDD per 1 000 inhabitants and per day



Boxes indicate the lower and the upper quartiles. The bold lines indicate the medians. Whiskers indicate the minimum and maximum values. For 1997–2009, only data from ESAC participating countries that also participated in ESAC-Net in 2012 are included. The number of participating countries is shown in parentheses.

Discussion

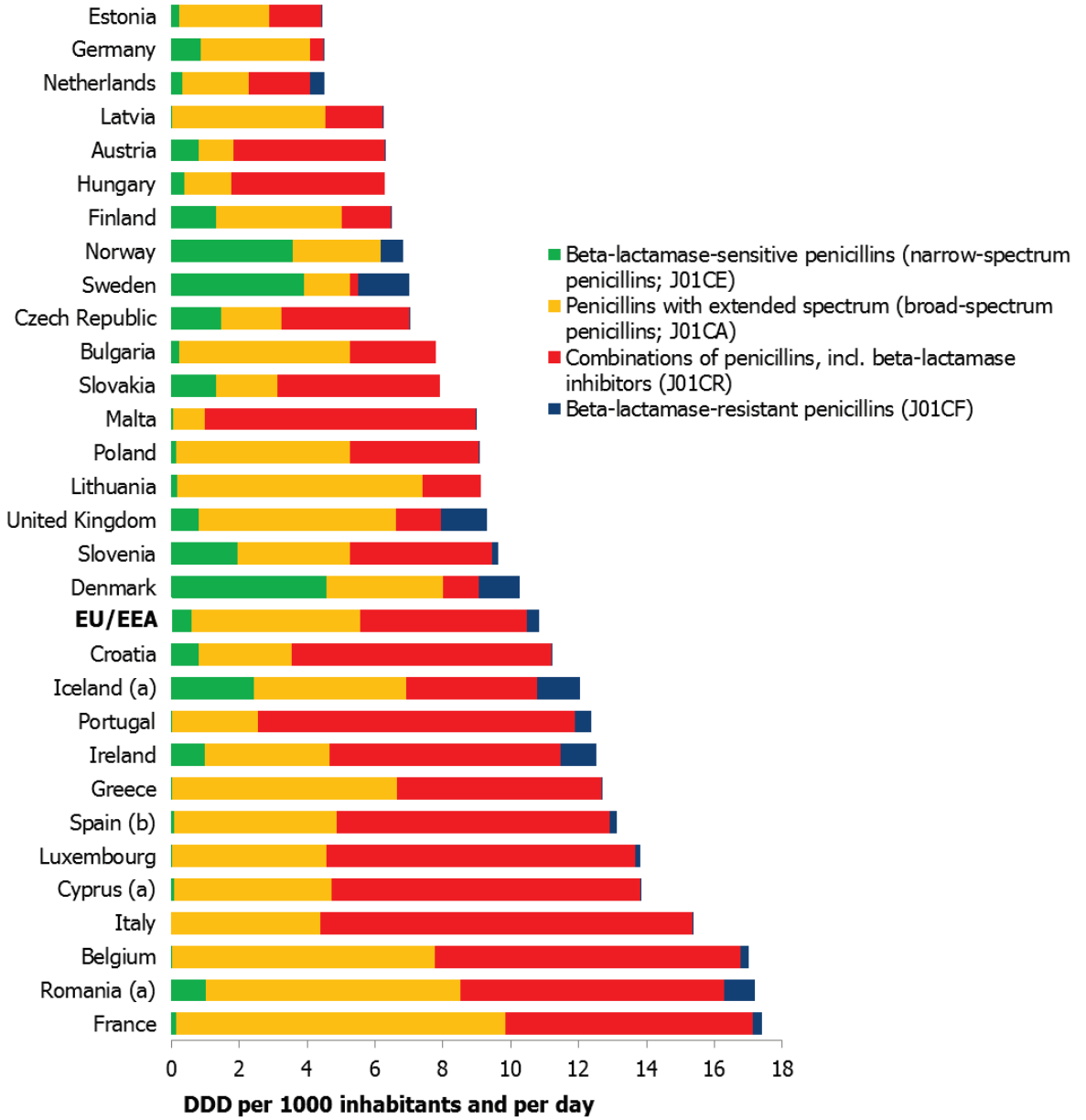
The ESAC project reported a significant decrease in consumption of tetracyclines (J01A) in the community during the period 1997–2009 [12]. However, the EU/EEA population-weighted mean consumption of tetracyclines in the reporting EU/EEA countries did not increase or decrease during the following period, 2008–2012, although national trends in some countries (less than 20%) included in the analyses did show a significant decrease in consumption of tetracyclines (J01A) over those five years.

3.1.3 Beta-lactams, penicillins (ATC group J01C)

Results

Penicillins (ATC subgroup J01C) were the most consumed antibacterial in the community in all EU/EEA countries. In 2012, consumption of penicillins ranged from 4.4 DDD per 1 000 inhabitants and per day (Estonia) to 17.4 DDD per 1 000 inhabitants and per day (France) (Table 3.1, Figure 3.1). The EU/EEA population-weighted mean consumption was 10.8 DDD per 1 000 inhabitants and per day among the countries reporting data for 2012. In 13 out of 30 countries, penicillins contributed to 50% or more of the total consumption of antibacterials for systemic use (ATC group J01) in the community, with Slovenia having the highest percentage (67% of the total antimicrobial consumption in the community) and Germany the lowest percentage (30%).

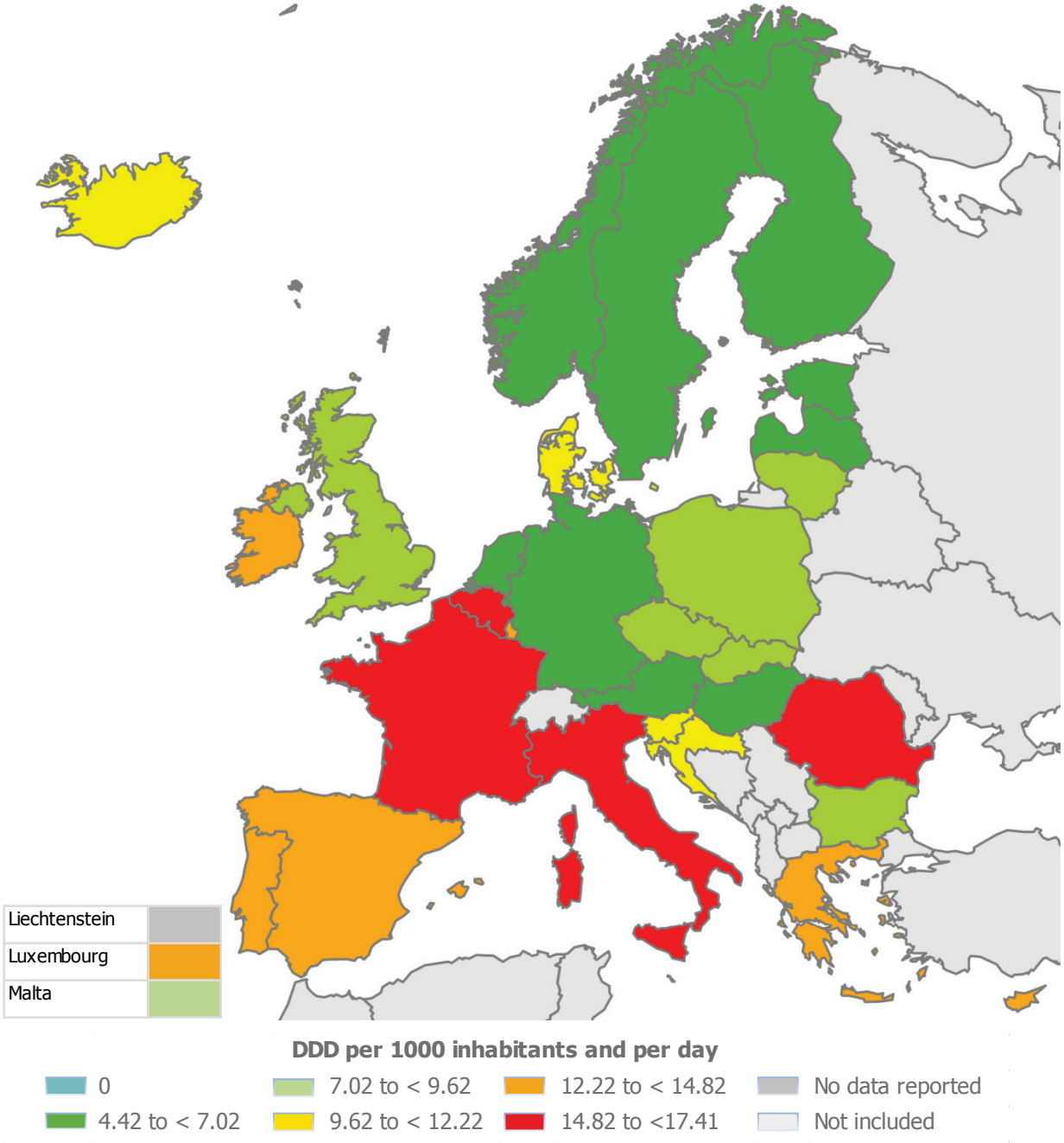
Figure 3.7. Consumption of broad- and narrow-spectrum penicillins in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day



(a) Cyprus, Iceland 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.

As shown in Figure 3.7, the main subgroups of penicillins in most of the EU/EEA countries were penicillins with extended spectrum (ATC group J01CA) and combinations of penicillins, including beta-lactamase inhibitors (ATC group J01CR). There is one exception; the Nordic countries, Denmark Norway and Sweden, reported the highest consumption of penicillins for the group of beta-lactamase-sensitive penicillin (ATC group J01CE). In these three countries, the relative consumption for ATC group J01CE from all penicillins was 46%, 53%, and 56%, respectively. In 2012, consumption of penicillins with extended spectrum (ATC group J01CA) ranged from 0.9 (Malta) to 9.7 (France) DDD per 1 000 inhabitants and per day. Consumption of combinations of penicillins, including beta-lactamase inhibitors (ATC group J01CR) ranged from 0.003 DDD per 1 000 inhabitants and per day (Norway) to 11.0 DDD per 1 000 inhabitants and per day (Italy).

Figure 3.8. Consumption of beta-lactams, penicillins (ATC group J01C) in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day



Cyprus, Iceland 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.
For more information on the map scales, see Chapter 2.3.

Consumption of amoxicillin (J01CA04, i.e. without enzyme inhibitor) ranged from 0.9 DDD per 1 000 inhabitants and per day (Sweden) to 9.7 DDD per 1 000 inhabitants and per day (France). Consumption of amoxicillin with enzyme inhibitor (J01CR02) ranged from 0.003 (Norway) to 10.3 (Italy) DDD per 1 000 inhabitants and per day.

Phenoxymethylpenicillin (J01CE02) was the most consumed beta-lactamase-sensitive penicillin in only three countries (Denmark, Norway and Sweden). Consumption of phenoxymethylpenicillin in these three countries accounted for half of the total consumption of this antibiotic in the 30 EU/EEA countries reporting data to ESAC-Net in 2012.

The proportion of combinations of penicillins, including beta-lactamase inhibitors (ATC group J01CR) among all beta-lactams, penicillins (ATC group J01C) ranged from 0.04% (Norway) to 89% (Malta).

In 2012, more than 50% of the consumption of antibacterials for systemic use (ATC group J01) in the community was made up of 12 different antibacterial agents. Of these agents, six were penicillins (ATC group J01C) (see Chapter 3.1.1).

Trends

Consumption of penicillins (ATC group J01C) significantly increased in six countries (Belgium, France, Latvia, Portugal, Spain and the United Kingdom) and none of the participating countries reported a significant decrease during 2008-2012 (Table 3.5). The EU/EEA population-weighted mean consumption of beta-lactams, penicillins (ATC group J01C) did not change between 2011 and 2012 (10.8 DDD per 1 000 inhabitants and per day).

Four countries (Latvia, Norway, Spain and the United Kingdom) reported a significant increase in the consumption of penicillins with extended spectrum (ATC group J01CA) whereas three countries (Cyprus, Italy and Malta) reported a significant decrease in the consumption of this group. The EU/EEA population-weighted mean consumption of this group did not change significantly.

The United Kingdom reported a significant increase in the consumption of beta-lactamase-sensitive penicillins (ATC group J01CE) and seven countries (Austria, Belgium, Bulgaria, Italy, Latvia, Luxembourg and the Netherlands) reported a significant decrease in the consumption of this group of penicillins. The EU/EEA population-weighted mean consumption did not change significantly.

Nine countries reported a significant increase or decrease in consumption of beta-lactamase-resistant penicillins (ATC group J01CF). Consumption of this group increased in Denmark, the Netherlands, Norway, Spain and the United Kingdom, and decreased in France, Germany, Italy and Malta. The EU/EEA population-weighted mean consumption increased significantly ($p<0.01$, average annual change: 0.01 DDD per 1 000 inhabitants and per day).

Consumption of combinations of penicillins, including beta-lactamase inhibitors (ATC group J01CR) significantly increased in ten countries (Denmark, Finland, France, Germany, Italy, Luxembourg, Portugal, Slovenia, Spain and the United Kingdom). None of the participating countries reported a significant decrease. The EU/EEA population-weighted mean consumption increased significantly ($p<0.02$, average annual change was 0.2 DDD per 1 000 inhabitants and per day).

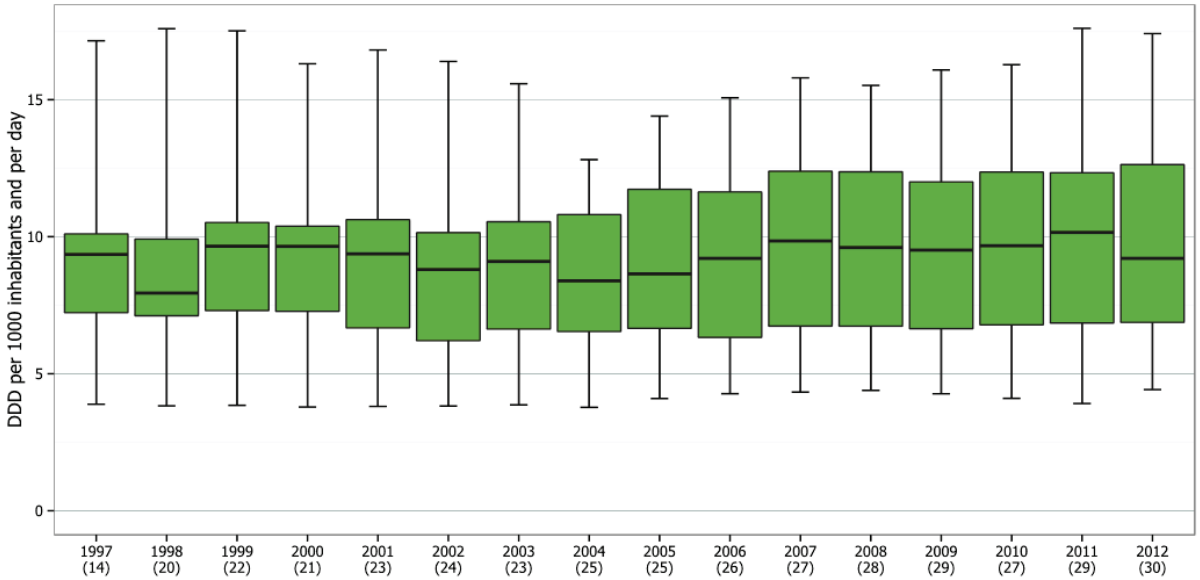
The trend in the consumption of penicillins (ATC group J01C) in the community since 1997 is shown in the boxplots of Figure 3.9. The median consumption in 2012 was lower by 1 DDD per 1 000 inhabitants and per day than in 2011. This is due to the fact that 19 countries reported lower consumption for 2012 than for 2011. However, as consumption increased or remained stable in the more populated EU/EEA countries, the population-weighted EU/EEA mean did not significantly change (Table 3.5).

Table 3.5. Trends of consumption of beta-lactams, penicillins (ATC group J01C) in the community, EU/EEA countries, 2008–2012, expressed as DDD per 1 000 inhabitants and per day

Country	2008	2009	2010	2011	2012	Trends in antimicrobial consumption, 2008–2012	Average annual change 2008–2012	Statistical significance
Estonia	4.7	4.4	4.2	4.6	4.4		-0.04	n.s.
Germany	4.4	4.3	4.1	3.9	4.5		-0.02	n.s.
Netherlands	4.4	4.5	4.4	4.5	4.5		0.01	n.s.
Latvia	5.2	5.0	5.6	6.1	6.2		0.32	significant
Austria	6.6	6.6	6.6	6.5	6.3		-0.08	n.s.
Hungary (c)	6.2	7.1	6.8	6.7	6.3			n.a.
Finland	6.1	6.1	6.6	6.6	6.5		0.14	n.s.
Norway	6.8	6.6	6.8	6.8	6.8		0.04	n.s.
Sweden	7.4	7.0	7.1	7.1	7.0		-0.07	n.s.
Czech Republic	7.3	7.7	7.6	8.1	7.0		-0.01	n.s.
Bulgaria	9.8	8.4	8.0	8.4	7.8		-0.40	n.s.
Slovakia (a)	9.4	9.6		9.3*	7.9			n.a.
Malta	9.0	9.1	9.8	10.2	9.0		0.10	n.s.
Poland (c)	10.2	10.7	9.4	11.7	9.1			n.a.
Lithuania	13.0*	10.1*	9.7*	10.4*	9.1			n.a.
United Kingdom	8.0	8.0	8.6	8.7	9.3		0.34	significant
Slovenia	9.4	9.5	9.7	9.7	9.6		0.06	n.s.
Denmark	9.9	9.9	10.3	10.9	10.3		0.18	n.s.
EU/EEA	**10.0**	**10.0**	**10.1**	**10.8**	**10.8**		**0.25**	**n.s.**
Croatia (a)					11.2			n.a.
Iceland	10.9	10.4	12.1*	12.1*	12.0*			n.a.
Portugal	11.6	12.0	12.1	12.3	12.4		0.18	significant
Ireland	11.4	10.7	10.7	12.2	12.5		0.39	n.s.
Greece	15.0*	12.9	12.9*	12.2	12.7			n.a.
Spain (b)	12.3	12.3	12.6	13.1	13.1		0.24	significant
Luxembourg	12.7	13.5	14.0	13.4	13.8		0.23	n.s.
Cyprus	14.9*	16.0*	14.4*	15.4*	13.8*		-0.27	n.s.
Italy	15.2	15.2	14.6	15.6	15.0		<0.01	n.s.
Belgium	15.5	15.1	16.3	16.6	17.0		0.44	significant
Romania (a)(b)(c)		4.3		17.6*	17.2*			n.a.
France	14.8	16.1	15.6	16.5	17.4		0.57	significant

**Total care data, including the hospital sector.*
(a) Croatia (2008–2011), Romania (2008 and 2010) and Slovakia (2010) did not report data for these years.
(b) Spain (2008–2012) and Romania (2009) reported reimbursement data, i.e. not including consumption without a prescription and other non-reimbursed courses.
(c) Hungary, Poland and Romania changed the type of data reported between 2008 and 2012 (reimbursement versus sales data).
EU/EEA refers to the corresponding population-weighted mean consumption.
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 2008 and 2012.
n.s.: not significant.

Figure 3.9. Trends and inter-country variations of consumption of beta-lactams, penicillins (ATC group J01C) in the community, EU/EEA countries, 1997-2012, expressed as DDD per 1 000 inhabitants and per day



Boxes indicate the lower and the upper quartiles. The bold lines indicate the medians. Whiskers indicate the minimum and maximum values. For 1997–2009, only data from ESAC participating countries that also participated in ESAC-Net in 2012 are included. The number of participating countries is shown in parentheses.

Discussion

Penicillins (ATC group J01C) are the most frequently prescribed and consumed antibacterials for systemic use in the community. The percentage of total consumption of antibacterials for systemic use (ATC group J01) corresponding to penicillins (ATC group J01C) has been suggested as a quality indicator for consumption in the community (Table 3.6).

Phenoxymethylpenicillin (ATC J01CE02) is the most commonly consumed penicillin in Denmark, Norway and Sweden, where it is used as a first-line drug among the penicillins, whereas in other countries amoxicillin (J01CA04) and amoxicillin with enzyme inhibitor (J01CR02) are the most commonly consumed penicillins.

Over the period 2008–2012, two thirds of the countries included in the national trend analyses showed a significant increase in the consumption of broad-spectrum penicillins, either penicillins with extended spectrum (ATC group J01CA) or combinations of penicillins, including beta-lactamase inhibitors (ATC group J01CR). Conversely, the consumption of narrow-spectrum penicillins (as defined by the quality indicator of the ESAC project, see Chapter 3.3), beta-lactamase-sensitive penicillins (ATC group J01CE) decreased significantly in less than half of the countries. Interestingly, the use of beta-lactamase-sensitive penicillins (ATC group J01CE) significantly increased in the United Kingdom.

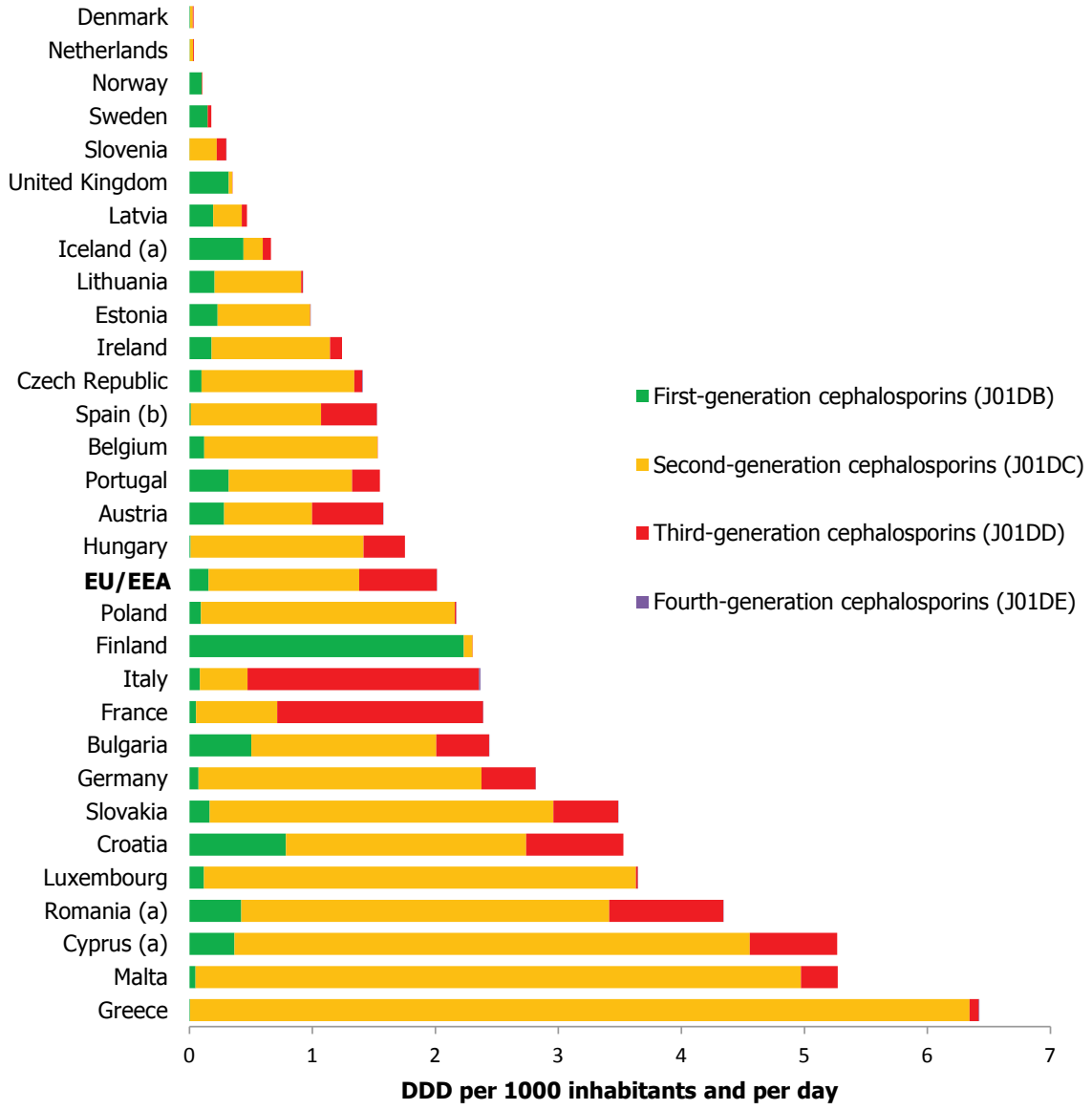
The ESAC project reported an overall significant increase in the consumption of penicillins (ATC group J01C) during the period 1997-2009 [13]. This increase, however, seems to have stopped as shown by the EU population-weighted mean consumption that did not change significantly between 2008 and 2012.

3.1.4 Other beta-lactam antibacterials (ATC group J01D)

Results

As shown in Figure 3.1 and Table 3.1, in 2012 the consumption of other beta-lactam antibacterials (ATC group J01D), the group which includes cephalosporins, ranged from 0.03 DDD per 1 000 inhabitants and per day (Denmark) to 6.5 DDD per 1 000 inhabitants and per day (Greece), with an EU/EEA population-weighted mean of 2.0 DDD per 1 000 inhabitants and per day. All countries except Cyprus, Greece, Malta and Romania reported a consumption of less than 3.9 DDD per 1 000 inhabitants and per day (Table 3.1, Figure 3.11). The proportion of consumption of cephalosporins (ATC groups J01DB–DE) out of the total consumption of antibacterials for systemic use (ATC group J01) ranged from 0.2% (Denmark) to 23.5% (Malta). No country reported consumption of other cephalosporins and penems (ATC group J01DI) in 2012.

Figure 3.10. Consumption of first-, second-, third- and fourth-generation cephalosporins (ATC groups J01DB–DE) in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day



(a) Cyprus, Iceland 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.

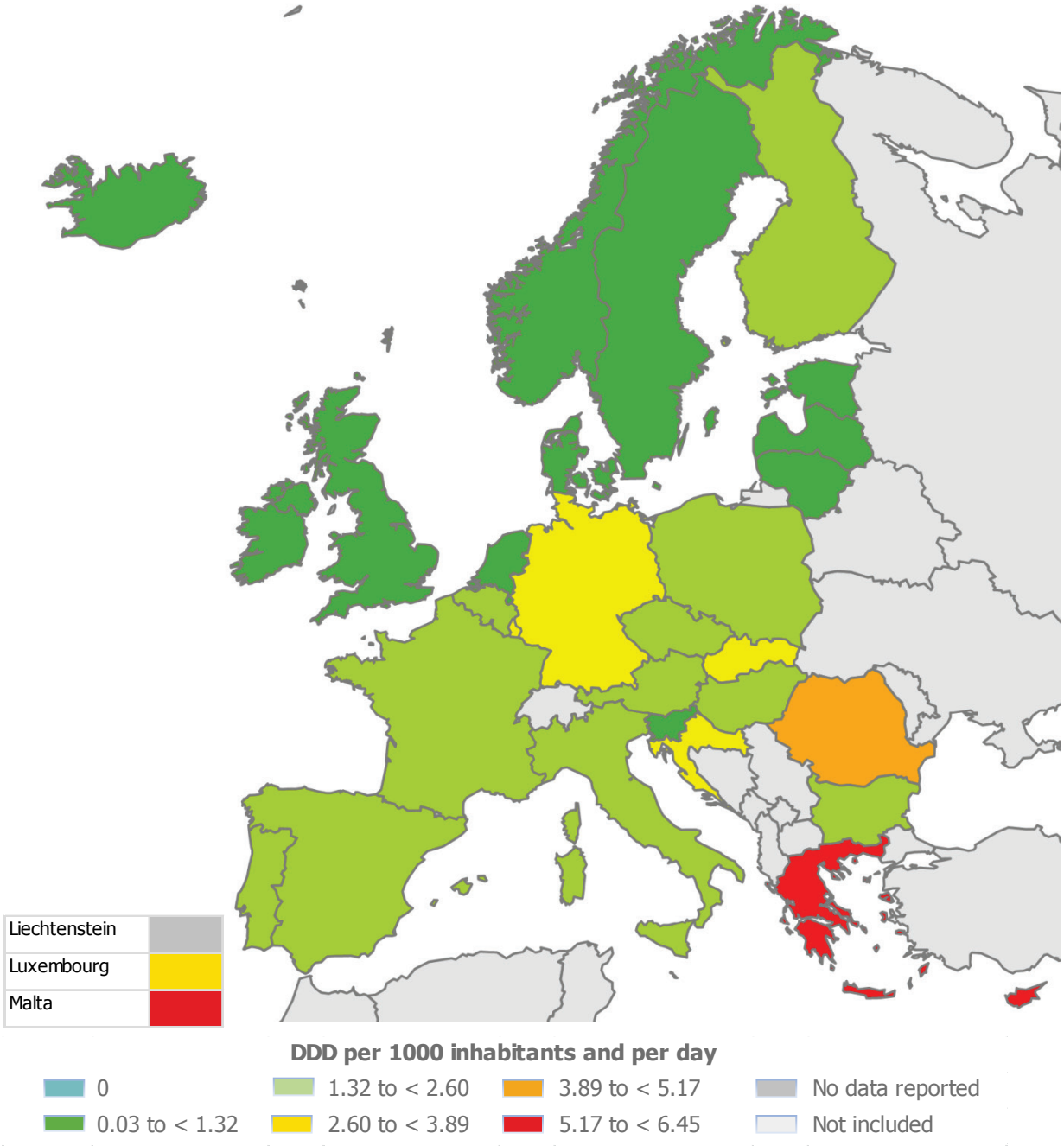
In 2012, the EU/EEA population-weighted mean proportion of first-generation cephalosporins (ATC group J01DB) among cephalosporins was 7.8% in the community. Consumption of first-generation cephalosporins ranged from 0.01 DDD per 1 000 inhabitants and per day (Slovenia) to 2.3 DDD per 1 000 inhabitants and per day (Finland) (Figure 3.10).

As shown in Figure 3.10, second-generation cephalosporins (ATC group J01DC) were the most frequently consumed subgroup of cephalosporins. In 2012, consumption of second-generation cephalosporins ranged from <0.001 DDD per 1 000 inhabitants and per day (Sweden) to 6.3 DDD per 1 000 inhabitants and per day (Greece).

In 2012, the highest consumption of third-generation cephalosporins (ATC group J01DD) was reported as 1.7 DDD per 1 000 inhabitants and per day in France and 1.9 DDD per 1 000 inhabitants and per day in Italy. In these two countries, third-generation cephalosporins accounted for more than two thirds of all cephalosporin consumption.

In 2012, consumption of fourth-generation cephalosporins (ATC group J01DE) was very low in EU/EEA countries. The highest consumption was reported as 0.009 DDD per 1 000 inhabitants and per day (Italy); 14 countries did not report any consumption.

Figure 3.11. Consumption of other beta-lactam antibacterials (ATC group J01D) in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day



Cyprus, Iceland 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.
For more information on the map scales, see Chapter 2.3.

Table 3.6. Trends of consumption of other beta-lactam antibacterials (ATC group J01D) in the community, EU/EEA countries, 2008–2012, expressed as DDD per 1 000 inhabitants and per day

Country	2008	2009	2010	2011	2012	Trends in antimicrobial consumption, 2008–2012	Average annual change 2008–2012	Statistical significance
Denmark	0.03	0.03	0.03	0.05	0.03		<0.01	n.s.
Netherlands	0.04	0.04	0.04	0.04	0.04		<0.01	n.s.
Norway	0.14	0.13	0.12	0.12	0.11		-0.01	significant
Sweden	0.30	0.24	0.20	0.18	0.18		-0.03	significant
Slovenia	0.44	0.42	0.40	0.33	0.30		-0.04	significant
United Kingdom	0.71	0.58	0.55	0.42	0.35		-0.09	significant
Latvia	0.51	0.45	0.57	0.50	0.47		<0.01	n.s.
Iceland	0.26	0.30	0.62*	0.63*	0.70*			n.a.
Lithuania	3.21*	1.27*	1.09*	1.32*	0.92			n.a.
Estonia	0.85	0.83	0.88	0.98	0.98		0.04	significant
Ireland	1.57	1.33	1.21	1.21	1.24		-0.08	n.s.
Czech Republic	1.39	1.55	1.62	1.51	1.44		0.01	n.s.
Spain (b)	1.66	1.56	1.56	1.53	1.52		-0.03	n.s.
Belgium	2.02	1.82	1.59	1.52	1.53		-0.13	significant
Portugal	1.99	1.96	1.81	1.65	1.55		-0.12	significant
Austria	1.70	1.80	1.70	1.65	1.58		-0.04	n.s.
Hungary (c)	1.86	1.98	1.95	1.95	1.75			n.a.
EU/EEA	**2.02**	**2.16**	**2.05**	**2.10**	**2.02**		**-0.01**	**n.s.**
Poland (c)	2.21	2.89	2.44	2.56	2.17			n.a.
Finland	2.33	2.33	2.33	2.36	2.30		<0.01	n.s.
Italy	2.78	2.78	2.55	2.53	2.31		-0.12	significant
France	2.54	2.92	2.67	2.55	2.39		-0.07	n.s.
Bulgaria	2.08	2.30	2.32	2.56	2.44		0.10	n.s.
Germany	1.93	2.39	2.61	2.72	2.82		0.21	significant
Slovakia (a)	3.92	4.12		3.89*	3.49*			n.a.
Croatia (a)					3.53			n.a.
Luxembourg	4.23	4.33	4.18	3.79	3.65		-0.17	significant
Romania (a)(b)(c)		2.47		3.86*	4.36			n.a.
Malta	4.90	5.50	5.04	5.68	5.27		0.09	n.s.
Cyprus	6.58*	6.45*	5.41*	6.07*	5.37*		-0.28	n.s.
Greece	9.54*	8.68	8.91*	7.60	6.45			n.a.

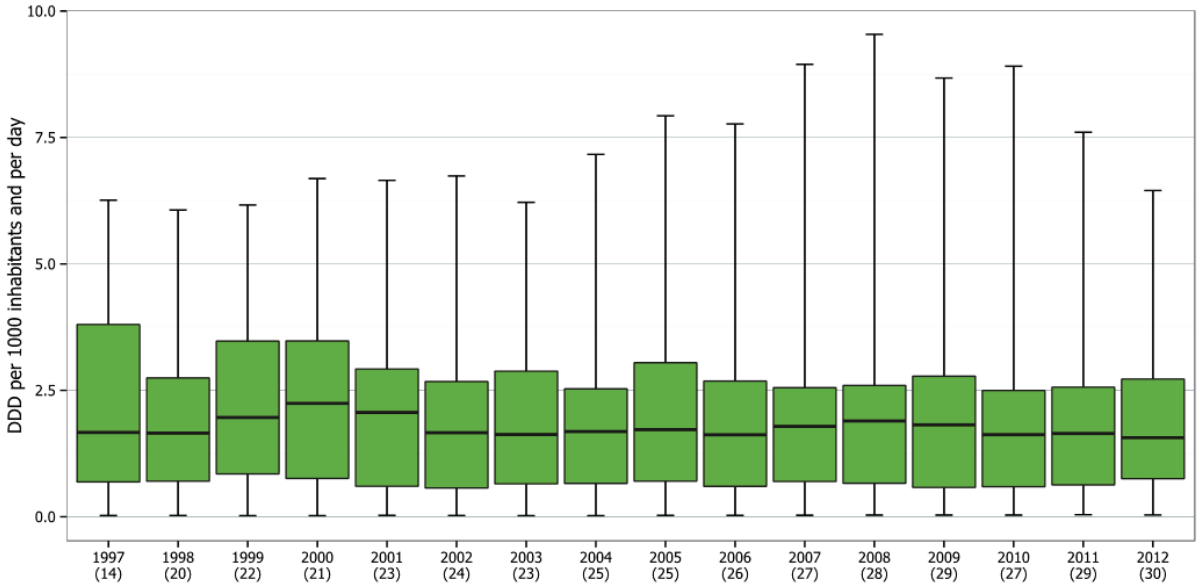
**Total care data, including the hospital sector.*
(a) Croatia (2008–2011), Romania (2008 and 2010) and Slovakia (2010) did not report data for these years.
(b) Spain (2008–2012) and Romania (2009) reported reimbursement data, i.e. not including consumption without a prescription and other non-reimbursed courses.
(c) Hungary, Poland and Romania changed the type of data reported between 2008 and 2012 (reimbursement versus sales data).
EU/EEA refers to the corresponding population-weighted mean consumption.
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 2008 and 2012.
n.s.: not significant.

Trends

Community consumption of other beta-lactam antibacterials (ATC group J01D) increased significantly in two countries (Estonia and Germany) and decreased significantly in eight countries (Belgium, Italy, Luxembourg, Norway, Portugal, Slovenia, Sweden and the United Kingdom) during 2008-2012 (Table 3.6).

For first-generation cephalosporins (ATC group J01DB), none of the countries showed a significant increase in consumption, whereas ten countries (Belgium, Bulgaria, Cyprus, France, Germany, Ireland, Italy, Norway, Poland, and the United Kingdom) showed a significant decrease in consumption of this group. The EU/EEA population-weighted mean consumption decreased significantly during 2008–2012 (p=0.009, average annual change was -0.02).

Figure 3.12. Trends and inter-country variations of consumption of other beta-lactam antibacterials (ATC group J01D) in the community, EU/EEA countries, 1997–2012, expressed as DDD per 1 000 inhabitants and per day



Boxes indicate the lower and the upper quartiles. The bold lines indicate the medians. Whiskers indicate the minimum and maximum values. For 1997–2009, only data from ESAC participating countries that also participated in ESAC-Net in 2012 are included. The number of participating countries is shown in parentheses.

Three countries (Bulgaria, Estonia and Germany) showed a significant increase in the consumption of second-generation cephalosporins (ATC group J01DC), whereas seven countries (Belgium, Italy, Luxembourg, Portugal, Slovenia, Sweden and the United Kingdom) showed a significant decrease.

Four countries (Belgium, Bulgaria, Estonia and Malta) showed a significant increase in the consumption of third-generation cephalosporins (ATC group J01DD) and four countries (Austria, Slovenia, Spain and the United Kingdom) showed a significant decrease.

Austria, France, Germany, Luxembourg and Spain showed a significant increase in the consumption of fourth-generation cephalosporins (ATC group J01DE). However, the consumption reported in these countries in 2012 was very low: < 0.0002 DDD per 1 000 inhabitants and per day. No country showed a significant decrease.

Four countries (France, Germany, Luxembourg and the United Kingdom) showed a significant increase in the consumption of carbapenems (ATC group J01DH) in the community whereas no country showed a significant decrease.

The EU/EEA population-weighted mean consumption neither decreased nor increased significantly for ATC groups J01DC, J01DD and J01DE.

The trend in the community consumption of other beta-lactam antibacterials (ATC group J01D) since 1997 is shown in Figure 3.12. The median consumption in 2012 was at a similar level to that for2011.

Discussion

The ESAC project reported a significant increase in the consumption of other beta-lactam antibacterials (ATC group J01D) between 1997 and 2009 [14]. For the period 2008–2012, however, the EU/EEA population-weighted mean consumption for that group did not increase or decrease significantly (Table 3.6).

Consumption of other beta-lactam antibacterials (ATC J01D), as presented in this chapter, includes a mix of various beta-lactams, from narrow-spectrum first-generation cephalosporins and monobactams, to broader-spectrum cephalosporins, and finally carbapenems which are generally considered as last-line antimicrobials.

Over the period 2008–2012, the overall consumption of other beta-lactam antibacterials (ATC group J01D) decreased significantly in one third of the countries included in the trend analyses. This was mainly due to a decrease in consumption of the first- and second-generation cephalosporins (ATC groups J01DB and J01DC).

Carbapenems (ATC group J01DH) are last-line antibacterials that are only administered parenterally. Their consumption in the community significantly increased in nearly one fifth of the countries during the period 2008–2012.

Greece reported the highest consumption of other beta-lactam antibacterials (ATC J01D) both in 2011 and 2012 but the country reported approximately 15% lower consumption of this group in 2012 than in 2011. For possible explanations for the decrease of antimicrobial consumption in the community in Greece, see Chapter 3.1.1.

The percentage of total consumption of antibacterials for systemic use (ATC group J01) corresponding to third- plus fourth-generation cephalosporins (ATC groups J01DD & J01DE) has been suggested as a quality indicator for consumption in the community (Table 3.15). Results from the former ESAC project suggest that variations in the consumption of second- and third-generation cephalosporins between countries and over time could be an indication of inappropriate use [14].

3.1.5 Sulfonamides and trimethoprim (ATC group J01E)

Results

In 2012, consumption of sulfonamides and trimethoprim (ATC J01E) ranged from 0.198 DDD per 1 000 inhabitants and per day (Malta) to 1.5 DDD per 1 000 inhabitants and per day (Poland), with an EU/EEA population-weighted mean of 0.7 DDD per 1 000 inhabitants and per day (Tables 3.1 and 3.7). The proportion of sulfonamide and trimethoprim consumption out of the total consumption of antibacterials for systemic use (ATC group J01) ranged from 0.9% (Malta) to 7.5% (Poland).

In 2012, the most consumed agents from ATC group J01E in the community were trimethoprim (J01EA01) alone and the combination of sulfamethoxazole and trimethoprim (J01EE01), which together made up 96.1% of the consumption of this group. In Ireland and in the United Kingdom, three quarters of the consumption in this group were reported as trimethoprim (J01EA01) at 0.9 and 1.0 DDD per 1 000 inhabitants and per day, respectively.

Trends

Temporal trends in the consumption of sulfonamides and trimethoprim (ATC group J01E) are presented in Table 3.7. Among countries reporting data for the period 2008–2012, community consumption significantly decreased in seven countries (Austria, the Czech Republic, Germany, Italy, the Netherlands, Norway and Slovenia) (Table 3.7). The United Kingdom reported a significant increase in the consumption of this group. For the period 2008–2012, however, the EU/EEA population-weighted mean did not increase or decrease significantly.

Additionally, six countries (Austria, Czech Republic, Germany, Italy, the Netherlands and Slovenia) showed a significant decrease in the consumption of combinations of sulfonamides and trimethoprim, including derivatives (ATC group J01EE). The United Kingdom was the only country showing an increase in the consumption of this group. The EU/EEA population-weighted mean consumption did not change significantly during the period.

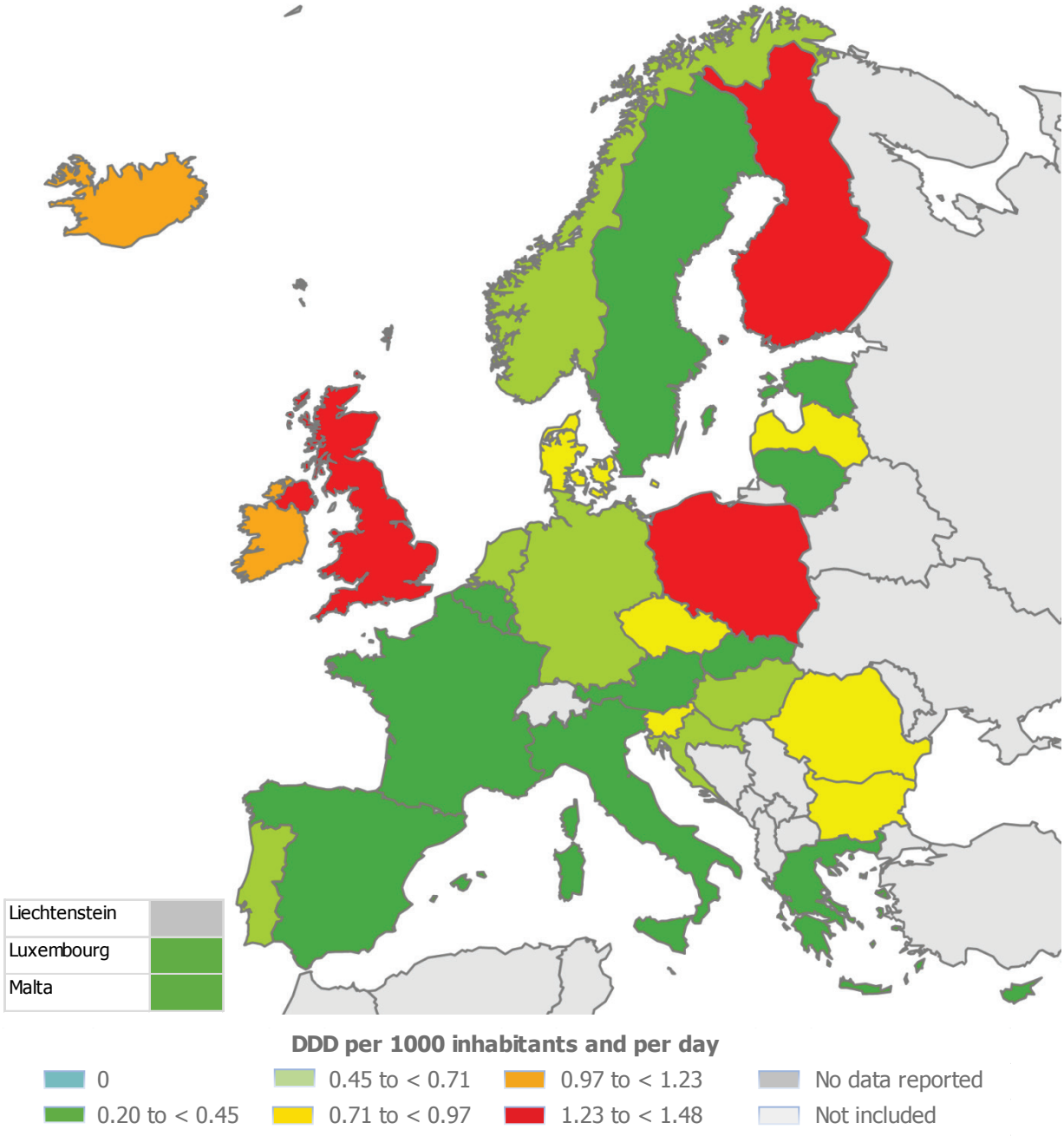
As shown in Figure 3.14, the median consumption of sulfonamides and trimethoprim (ATC group J01E) in EU/EEA countries has slowly decreased from 0.79 DDD in 2004 to 0.52 DDD per 1 000 inhabitants and per day in 2012.

Discussion

Consumption of sulfonamides and trimethoprim (ATC group J01E) is dominated by one substance, i.e. trimethoprim, used alone (ATC J01EA01) or in a combination with sulfamethoxazole (ATC J01EE01).

The large number of countries showing a significant decrease in the consumption of sulfonamides and trimethoprim (ATC group J01E) in the community between 2008 and 2012 is in line with the decreasing trend that was observed by the ESAC project for the period 1997-2009.

Figure 3.13. Consumption of sulfonamides and trimethoprim (ATC group J01E) in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day



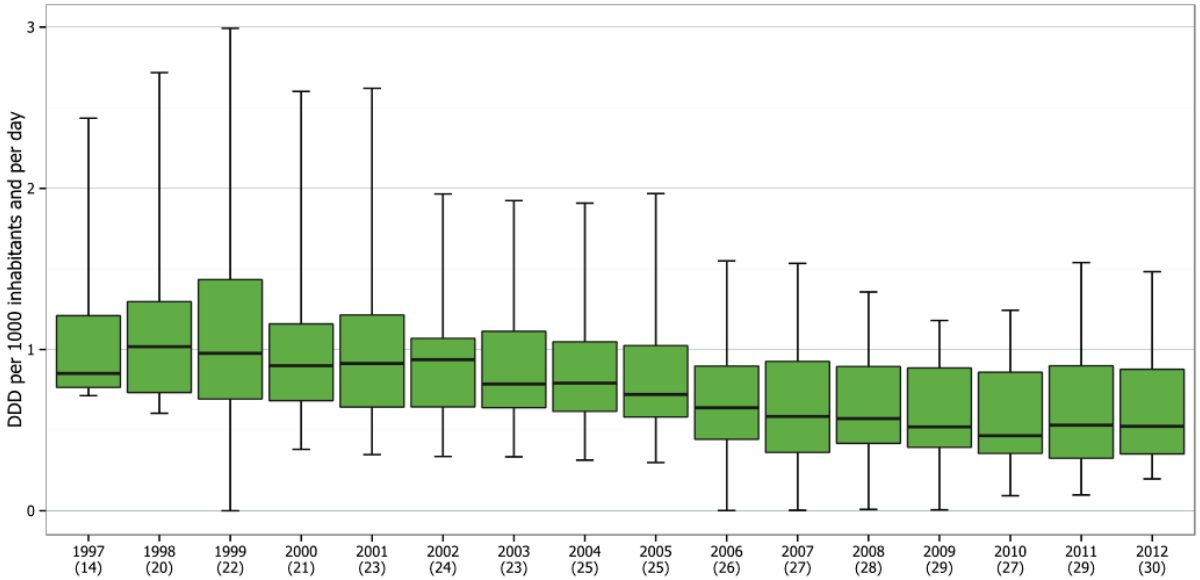
Cyprus, Iceland and Romania provided total care data, i.e. including the hospital sector.
Spain provided reimbursement data, i.e. not including consumption without a prescription and other non-reimbursed courses.
For more information on the map scales, see Chapter 2.3.

Table 3.7. Trends of consumption of sulfonamides and trimethoprim (ATC group J01E) in the community, EU/EEA countries, 2008–2012, expressed as DDD per 1 000 inhabitants and per day

Country	2008	2009	2010	2011	2012	Trends in antimicrobial consumption, 2008–2012	Average annual change 2008–2012	Statistical significance
Malta	0.2	0.2	0.2	0.3	0.2		0.01	n.s.
Austria	0.3	0.3	0.3	0.2	0.2		-0.02	significant
Belgium	0.4	0.4	0.3	0.3	0.3		-0.03	n.s.
Spain (b)	0.3	0.3	0.3	0.3	0.3		-0.01	n.s.
Greece	0.4*	0.4	0.3*	0.3	0.3			n.a.
Luxembourg	0.4	0.4	0.3	0.3	0.3		-0.01	n.s.
Slovakia (a)	0.5	0.4		0.4*	0.3			n.a.
Italy	0.5	0.5	0.4	0.4	0.3		-0.04	significant
Cyprus	0.4*	0.5*	0.4*	0.3*	0.4*		-0.03	n.s.
Lithuania	<0.1*	<0.1*	0.4*	0.4*	0.4			n.a.
Estonia	0.5	0.4	0.4	0.4	0.4		-0.02	n.s.
Sweden	0.6	0.5	0.4	0.5	0.4		-0.03	n.s.
France	0.5	0.4	0.4	0.4	0.4		-0.01	n.s.
Hungary (c)	0.7	0.7	0.6	0.5	0.5			n.a.
Netherlands	0.6	0.6	0.6	0.5	0.5		-0.01	significant
Portugal	0.4	0.4	0.5	0.7	0.5		0.04	n.s.
Germany	0.8	0.7	0.7	0.6	0.6		-0.06	significant
Croatia (a)					0.7			n.a.
EU/EEA	**0.7**	**0.6**	**0.6**	**0.5**	**0.7**		**-0.01**	**n.s.**
Norway	0.8	0.7	0.7	0.7	0.7		-0.02	significant
Czech Republic	0.9	0.9	0.9	0.8	0.7		-0.03	significant
Denmark	0.8	0.8	0.8	0.7	0.8		<0.01	n.s.
Bulgaria	1.0	0.9	0.9	0.9	0.8		-0.03	n.s.
Romania (a)(b)(c)		0.2		<0.1*	0.9*			n.a.
Slovenia	1.1	1.1	1.1	1.0	0.9		-0.04	significant
Latvia	0.9	1.1	0.9	1.0	1.0		0.01	n.s.
Iceland	1.4	1.1	0.9	1.0	1.0			n.a.
Ireland	1.0	1.1	1.1	1.2	1.2		0.04	n.s.
United Kingdom	1.1	1.2	1.2	1.3	1.3		0.05	significant
Finland	1.0	1.0	1.0	1.5	1.4		0.12	n.s.
Poland (c)	1.0	0.9	0.1	0.1	1.5			n.a.

**Total care data, including the hospital sector.*
(a) Croatia (2008–2011), Romania (2008 and 2010) and Slovakia (2010) did not report data for these years.
(b) Spain (2008–2012) and Romania (2009) reported reimbursement data, i.e. not including consumption without a prescription and other non-reimbursed courses.
(c) Hungary, Poland and Romania changed the type of data reported between 2008 and 2012 (reimbursement versus sales data).
EU/EEA refers to the corresponding population-weighted mean consumption.
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 2008 and 2012.
n.s.: not significant.

Figure 3.14. Trends and inter-country variations of consumption of sulfonamides and trimethoprim (ATC group J01E) in the community, EU/EEA countries, 1997–2012, expressed as DDD per 1 000 inhabitants and per day



Boxes indicate the lower and the upper quartiles. The bold lines indicate the medians. Whiskers indicate the minimum and maximum values. For 1997–2009, only data from ESAC participating countries that also participated in ESAC-Net in 2012 are included. The number of participating countries is shown in parentheses.

3.1.6 Macrolides, lincosamides and streptogramins (ATC group J01F)

Results

Macrolides, lincosamides and streptogramins (ATC group J01F) form the second most commonly used ATC subgroup in 18 of the reporting countries. In 2012, consumption ranged from 0.6 DDD per 1 000 inhabitants and per day (Sweden) to 7.7 DDD per 1 000 inhabitants and per day (Greece). The EU/EEA population-weighted mean consumption was 3.2 DDD per 1 000 inhabitants and per day.

The EU map displaying countries according to five equidistant intervals between the minimum and maximum values for 2012 data, shows Greece and Slovakia as the highest consumers of macrolides, lincosamides and streptogramins (ATC group J01F) with values higher than 4.9 DDD per 1 000 inhabitants and per day (i.e. in the last two intervals) (Table 3.1, Figure 3.16).

The proportion of consumption of macrolides, lincosamides and streptogramins (ATC group J01F) out of the total consumption of antibacterials for systemic use (ATC group J01 group) ranged from 4.4% (Sweden) to 24.5% (Slovakia).

Table 3.8. Consumption of short-, intermediate- and long-acting macrolides for systemic use in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day

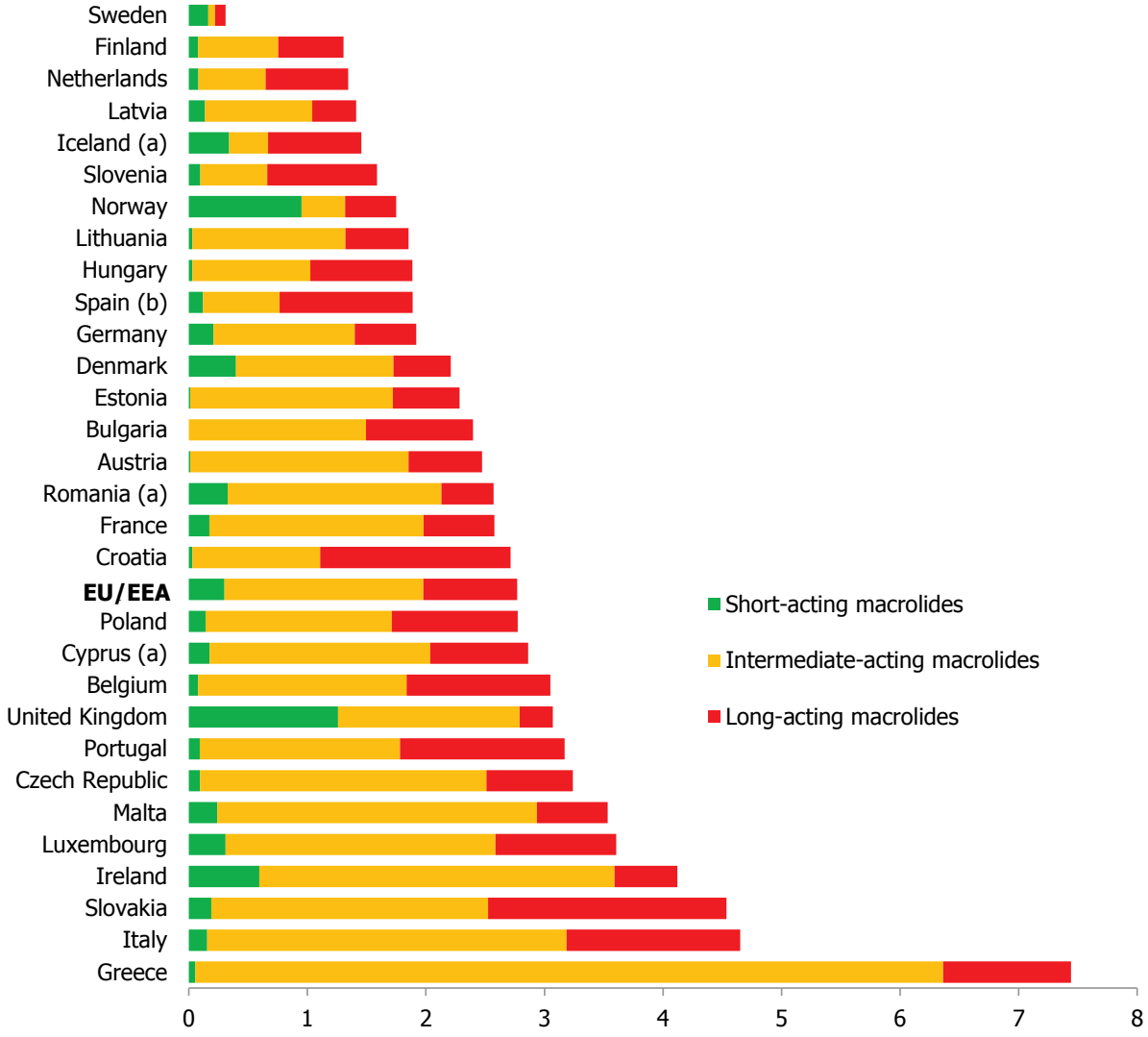
Country	Short-acting macrolides	Intermediate-acting macrolides	Long-acting macrolides	Total
Austria	0.01	1.84	0.62	2.47
Belgium	0.08	1.76	1.21	3.05
Bulgaria	0	1.50	0.90	2.40
Croatia	0.03	1.08	1.61	2.71
Cyprus (a)	0.18	1.86	0.82	2.86
Czech Republic	0.09	2.42	0.73	3.24
Denmark	0.40	1.33	0.48	2.21
Estonia	0.01	1.71	0.56	2.28
Finland	0.08	0.68	0.55	1.30
France	0.17	1.81	0.60	2.58
Germany	0.21	1.19	0.52	1.92
Greece	0.06	6.31	1.08	7.44
Hungary	0.03	1.00	0.86	1.89
Iceland (a)	0.34	0.33	0.79	1.46
Ireland	0.59	3.00	0.53	4.12
Italy	0.16	3.03	1.46	4.65
Latvia	0.14	0.90	0.37	1.41
Lithuania	0.03	1.29	0.53	1.85
Luxembourg	0.31	2.28	1.02	3.61
Malta	0.24	2.70	0.60	3.53
Netherlands	0.08	0.57	0.70	1.34
Norway	0.95	0.37	0.43	1.75
Poland	0.14	1.57	1.06	2.77
Portugal	0.09	1.69	1.39	3.17
Romania (a)	0.33	1.80	0.44	2.57
Slovakia	0.19	2.34	2.01	4.54
Slovenia	0.10	0.57	0.93	1.59
Spain (b)	0.12	0.64	1.12	1.89
Sweden	0.16	0.06	0.09	0.31
United Kingdom	1.26	1.53	0.28	3.07
EU/EEA mean (population-weighted)	**0.30**	**1.68**	**0.79**	**2.77**

A classification of macrolides is used as described by the ESAC project [8] according to the mean plasma elimination (Annex 1).
(a) Cyprus, Iceland 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.

In 2012, the overall consumption of macrolides (ATC group J01FA) varied by a factor of 25 from 0.3 DDD per 1 000 inhabitants and per day (Sweden) to 7.4 DDD per 1 000 inhabitants and per day (Greece) with an EU/EEA population-weighted mean consumption of 2.8 DDD per 1 000 inhabitants and per day (Table 3.8).

Among short-acting macrolides, two countries, Norway and the United Kingdom, reported the highest consumption of all reporting EU/EEA countries with 0.95 and 1.26 DDD per 1 000 inhabitants and per day. Erythromycin (ATC J01FA01) was the most consumed short-acting substance in Norway, Sweden and the United Kingdom, where the consumption of Erythromycin accounted for 54%, 53% and 41% of the total consumption of all macrolides (ATC group J01FA), respectively.

Figure 3.15. Consumption of short-, intermediate- and long-acting macrolides for systemic use in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day

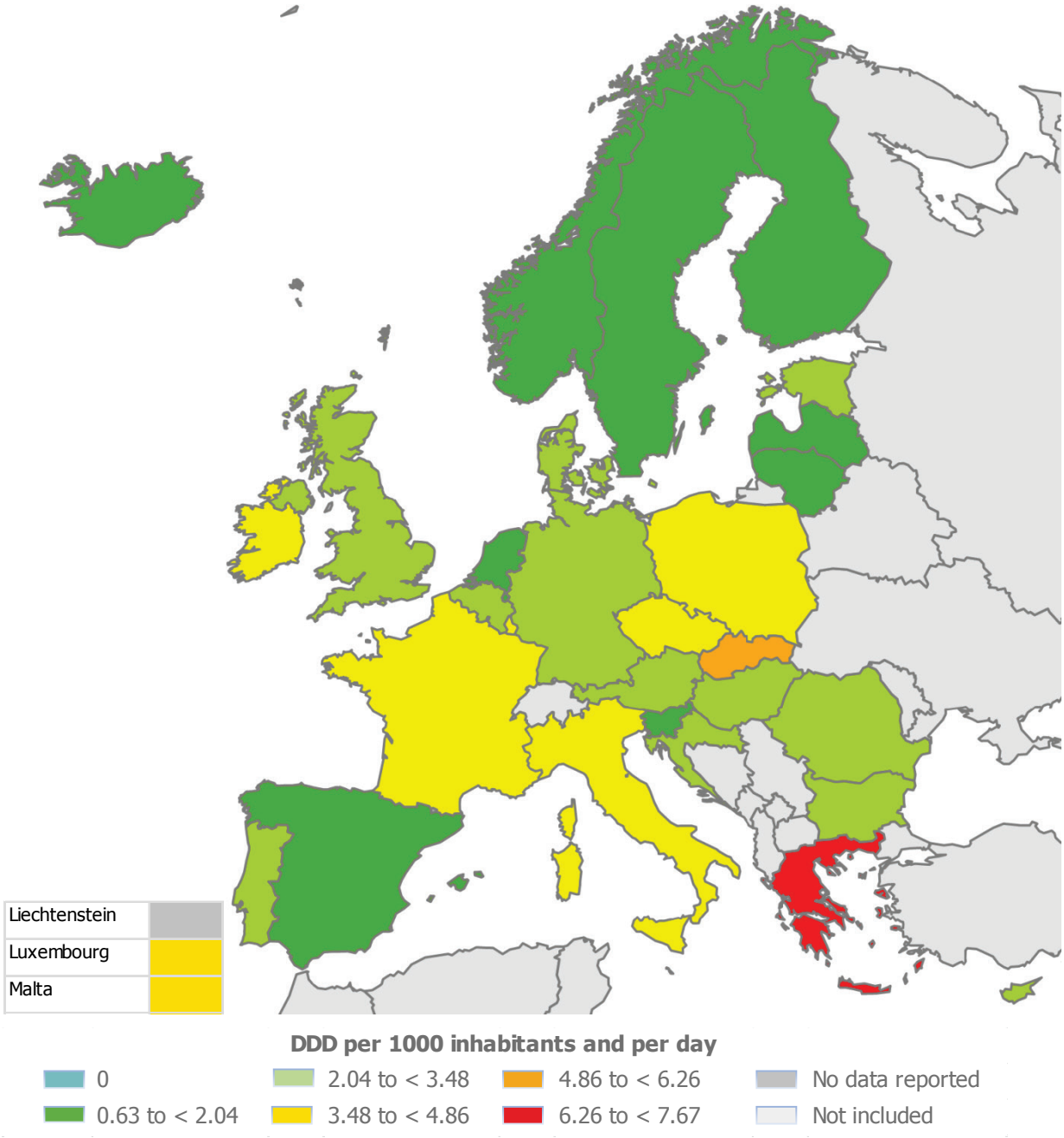


A classification of macrolides is used as described by the ESAC project [8] according to the mean plasma elimination (Annex 1).
(a) Cyprus, Iceland and Romania provided total care data, i.e. including the hospital sector.
(b) Spain provided reimbursement data, i.e. not including consumption without a prescription and other non-reimbursed courses.
EU/EEA refers to the corresponding population-weighted mean consumption.

Intermediate-acting macrolides, mostly clarithromycin (ATC J01FA09), accounted for 61% of the total consumption of macrolides (ATC group J01FA) with a consumption ranging from 0.06 DDD per 1 000 inhabitants and per day (Sweden) to 6.3 DDD per 1 000 inhabitants and per day (Greece).

Consumption of long-acting macrolides, mostly azithromycin (J01FA10), ranged from 0.09 DDD per 1 000 inhabitants and per day (Sweden) to 2.0 DDD per 1 000 inhabitants and per day (Slovakia).

Figure 3.16. Consumption of macrolides, lincosamides and streptogramins (ATC group J01F) in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day



Cyprus, Iceland 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.
For more information on the map scales, see Chapter 2.3.

Trends

Temporal trends in the consumption of macrolides, lincosamides and streptogramins (ATC group J01F) are presented in Table 3.9. Among countries reporting data for the period 2008–2012, community consumption of macrolides, lincosamides and streptogramins (ATC group J01F) significantly increased in four countries (Belgium, Latvia, Luxembourg and the United Kingdom), while only four countries (France, Italy, Portugal and Slovenia) reported a significant decrease in the consumption of this group. The EU/EEA population-weighted mean consumption neither increased, nor decreased significantly.

Table 3.9. Trends of consumption of macrolides, lincosamides and streptogramins (ATC group J01F) in the community, EU/EEA countries, 2008–2012, expressed as DDD per 1 000 inhabitants and per day

Country	2008	2009	2010	2011	2012	Trends in antimicrobial consumption, 2008–2012	Average annual change 2008–2012	Statistical significance
Sweden	0.4	0.8	0.7	0.6	0.6		0.02	n.s.
Netherlands	1.5	1.5	1.4	1.5	1.5		0.00	n.s.
Latvia	1.0	0.9	1.1	1.4	1.5		0.16	significant
Finland	1.4	1.5	1.5	1.8	1.6		0.06	n.s.
Iceland	1.6	1.2	1.6*	1.6*	1.7*			n.a.
Slovenia	2.4	2.2	2.1	2.0	1.8		-0.14	significant
Lithuania	2.0*	1.9*	1.7*	1.9*	1.9			n.a.
Spain (b)	1.9	1.9	2.0	2.1	2.0		0.03	n.s.
Norway	1.9	1.7	1.8	2.0	2.0		0.05	n.s.
Denmark	2.3	2.3	2.4	2.7	2.3		0.02	n.s.
Hungary (c)	3.1	3.0	3.0	2.7	2.4			n.a.
Estonia	2.3	2.1	2.2	2.5	2.4		0.07	n.s.
Romania (a)(b)(c)		1.8		2.9*	2.7*			n.a.
Germany	2.4	2.5	2.3	2.3	2.7		0.03	n.s.
Cyprus	3.5*	4.0*	2.9*	3.1*	2.9*		-0.20	n.s.
Croatia (a)					3.0			n.a.
Bulgaria	2.9	3.0	3.0	3.3	3.0		0.06	n.s.
United Kingdom	2.5	2.5	2.7	2.8	3.1		0.16	significant
Austria	3.7	3.9	3.6	3.4	3.2		-0.15	n.s.
EU/EEA	**3.3**	**3.3**	**3.2**	**3.2**	**3.2**		**-0.04**	**n.s.**
Portugal	3.9	3.8	3.4	3.4	3.2		-0.18	significant
Belgium	2.8	3.0	2.9	3.2	3.4		0.13	significant
Czech Republic	3.3	3.7	3.5	3.6	3.5		0.03	n.s.
Poland (c)	3.7	3.9	3.5	3.8	3.5			n.a.
Malta	3.7	3.9	3.1	3.7	3.7		-0.03	n.s.
France	4.2	4.1	3.8	3.8	3.7		-0.12	significant
Luxembourg	3.8	3.9	3.9	3.9	4.0		0.05	significant
Ireland	4.1	3.8	3.7	4.2	4.2		0.05	n.s.
Italy	5.3	5.3	5.0	5.0	4.6		-0.18	significant
Slovakia (a)	5.9	6.1		5.8*	4.9			n.a.
Greece	11.6*	11.5	8.8*	9.4	7.7			n.a.

**Total care data, including the hospital sector.*
(a) Croatia (2008–2011), Romania (2008 and 2010) and Slovakia (2010) did not report data for these years.
(b) Spain (2008–2012) and Romania (2009) reported reimbursement data, i.e. not including consumption without a prescription and other non-reimbursed courses.
(c) Hungary, Poland and Romania changed the type of data reported between 2008 and 2012 (reimbursement versus sales data).
EU/EEA refers to the corresponding population-weighted mean consumption.
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 2008 and 2012.
n.s.: not significant.

Belgium, Latvia and the United Kingdom showed a significant increase in the consumption of macrolides (ATC group J01FA), whereas five countries (Austria, France, Italy, Portugal and Slovenia) showed a significant decrease. No significant increase or decrease for the EU/EEA population-weighted mean consumption was observed.

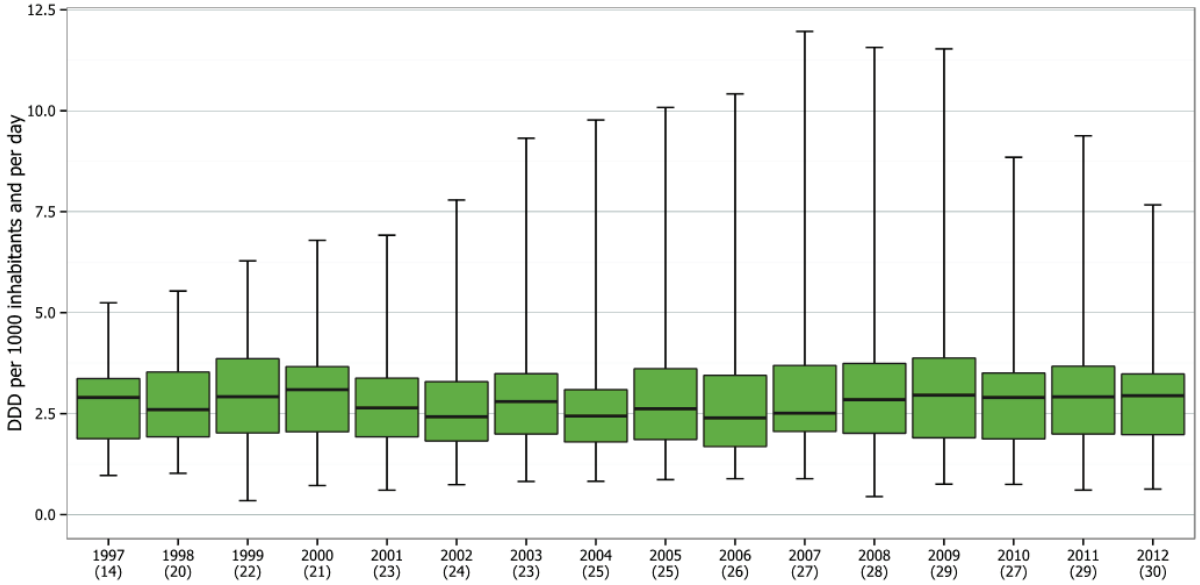
Ten countries (Belgium, Bulgaria, the Czech Republic, Denmark, Finland, Luxembourg, the Netherlands, Norway, Spain and the United Kingdom) showed a significant increase in the consumption of lincosamides (ATC group

J01FF). Italy reported a significant decrease in the consumption of this group. The EU/EEA population-weighted mean consumption neither decreased, nor increased significantly.

None of the countries showed a significant increase or decrease in the consumption of streptogramins (ATC group J01FG). The EU/EEA population-weighted mean consumption neither decreased nor increased significantly during 2008–2012.

The median consumption of macrolides, lincosamides and streptogramins (ATC group J01F) did not change between 2011 and 2012 and was reported at the same level as at the start of the surveillance in 1997, with 3.2 DDD per 1 000 inhabitants and per day (Figure 3.17).

Figure 3.17. Trends and inter-country variations of consumption of macrolides, lincosamides and streptogramins (ATC group J01F) in the community, EU/EEA countries, 1997–2012, expressed as DDD per 1 000 inhabitants and per day



Boxes indicate the lower and the upper quartiles. The bold lines indicate the medians. Whiskers indicate the minimum and maximum values. For 1997–2009, only data from ESAC participating countries that also participated in ESAC-Net in 2012 are included. The number of participating countries is shown in parentheses.

Discussion

Macrolides (ATC group J01FA), in particular intermediate-acting substances, were the most often consumed antibacterials of the group comprising macrolides, lincosamides and streptogramins (ATC group J01F) in all countries, with the exception of Sweden where lincosamides (ATC group J01FF) were predominantly used.

Nearly half of the countries showed a significant increase in the consumption of lincosamides (ATC group J01FF) during the five-year period 2008–2012.

A significant increase in the consumption of macrolides and of lincosamides, and of the ratio of long-acting to intermediate-acting macrolide consumption (compositional data analysis for ESAC project data from 1997 to 2009) has previously been reported by the former ESAC project for the period 1997–2009 [8]. This report shows that the EU/EEA population-weighted mean consumption of macrolides, lincosamides and streptogramins (ATC group J01F) did not change significantly between 2008 and 2012.

The large inter-country variation in the consumption of macrolides may indicate inappropriate use in some of the reporting countries.

3.1.7 Quinolone antibacterials (ATC group J01M)

Results

The pattern of community consumption of quinolone antibacterials (ATC group J01M) shows a gradient from northern to southern Europe (Figure 3.19). In 2012, consumption varied by a factor of 8.8 ranging from 0.4 DDD per 1 000 inhabitants and per day (United Kingdom) to 3.5 DDD per 1 000 inhabitants and per day (Cyprus), with an EU/EEA population-weighted mean consumption of 1.8 DDD per 1 000 inhabitants and per day

(Tables 3.1, 3.10). The proportion of consumption of quinolone antibacterials (ATC group J01M) out of the total consumption of antibacterials for systemic use (ATC group J01) ranged from 2.1% (United Kingdom) to 13.9% (Hungary).

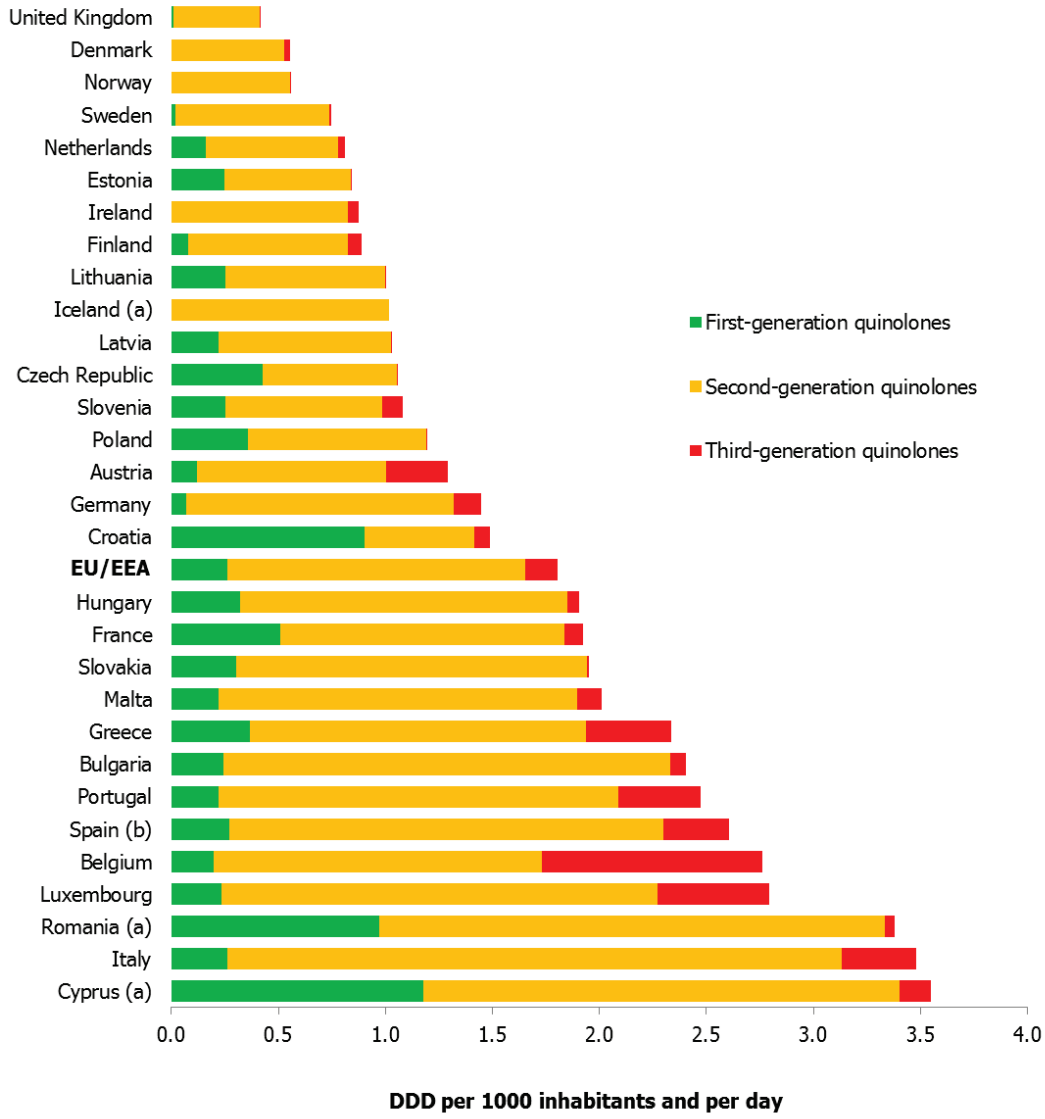
Table 3.10. Consumption of first-, second- and third-generation quinolones for systemic use in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day

Country	First-generation quinolones	Second-generation quinolones	Third-generation quinolones	Total
Austria	0.12	0.88	0.29	1.29
Belgium	0.20	1.54	1.03	2.76
Bulgaria	0.24	2.09	0.07	2.40
Croatia	0.90	0.51	0.07	1.49
Cyprus (a)	1.18	2.22	0.15	3.55
Czech Republic	0.43	0.63	<0.01	1.06
Denmark	0	0.53	0.03	0.55
Estonia	0.25	0.59	<0.01	0.84
Finland	0.08	0.74	0.07	0.89
France	0.51	1.33	0.09	1.92
Germany	0.07	1.25	0.13	1.45
Greece	0.36	1.57	0.40	2.33
Hungary	0.32	1.53	0.06	1.91
Iceland (a)	0	1.02	0	1.02
Ireland	<0.01	0.82	0.05	0.87
Italy	0.26	2.87	0.35	3.48
Latvia	0.22	0.81	<0.01	1.03
Lithuania	0.25	0.75	<0.01	1.00
Luxembourg	0.23	2.04	0.53	2.79
Malta	0.22	1.67	0.11	2.01
Netherlands	0.16	0.62	0.03	0.81
Norway	0	0.55	<0.01	0.56
Poland	0.36	0.83	<0.01	1.19
Portugal	0.22	1.87	0.38	2.47
Romania (a)	0.97	2.36	0.05	3.38
Slovakia	0.30	1.64	0.01	1.95
Slovenia	0.25	0.73	0.10	1.08
Spain (b)	0.27	2.03	0.31	2.61
Sweden	0.02	0.72	0.01	0.75
United Kingdom	0.01	0.40	0.01	0.42
EU/EEA mean (population-weighted)	**0.26**	**1.39**	**0.15**	**1.81**

A classification of quinolone antibacterials into three generations is used, based on their chemical structure and antimicrobial activity as described by the ESAC project [7] (Annex 1).
(a) Cyprus, Iceland 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.

In 2012, consumption of first-generation quinolones ranged from <0.01 DDD per 1 000 inhabitants and per day (Ireland) to 1.2 DDD per 1 000 inhabitants and per day (Cyprus). Denmark, Iceland and Norway did not report any consumption of first-generation quinolones (Table 3.10).

Figure 3.18. Consumption of first-, second- and third-generation quinolones for systemic use in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day

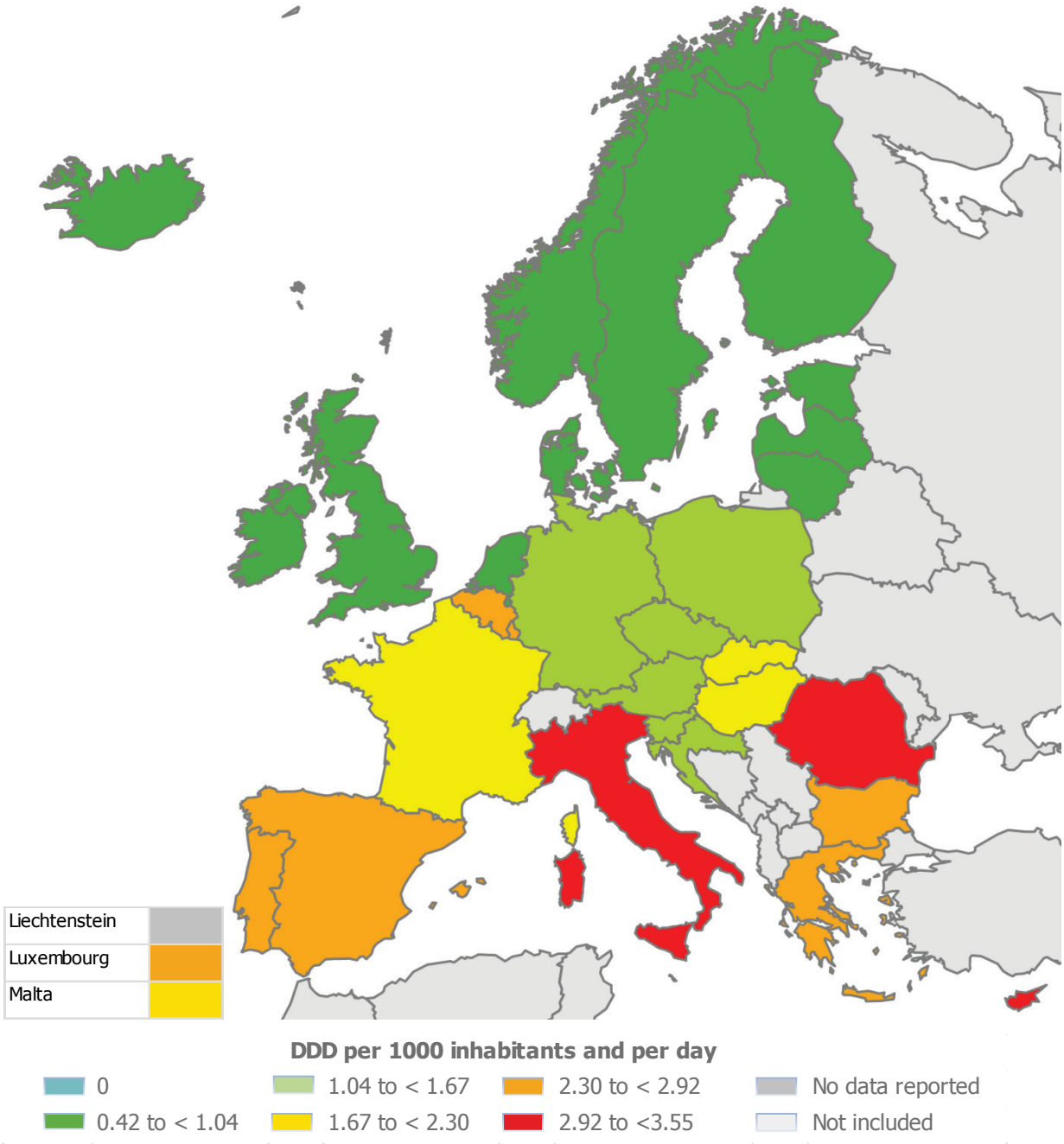


A classification of quinolone antibacterials into three generations is used based on their chemical structure and antimicrobial activity as described by the ESAC project [7] (Annex 1).
(a) Cyprus, Iceland and Romania provided total care data, i.e. including the hospital sector.
(b) Spain provided reimbursement data, i.e. not including consumption without a prescription and other non-reimbursed courses.
EU/EEA refers to the corresponding population-weighted mean consumption.

In 2012, second-generation quinolones were consumed on average three times more often than first- and third-generation quinolones together. Ciprofloxacin (J01MA02) accounted for 71% of the consumption of second-generation quinolones in all countries. The lowest consumption of ciprofloxacin was reported from the United Kingdom and the highest from Luxembourg with 0.35 and 1.7 DDD per 1 000 inhabitants and per day, respectively.

The proportion of consumption of third-generation quinolones out of the total consumption of quinolone antibacterials (ATC J01M) varied from 0.03% in Poland to 37.3% in Belgium.

Figure 3.19. Consumption of quinolone antibacterials (ATC group J01M) in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day



Cyprus, Iceland 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.
For more information on the map scales, see Chapter 2.3.

Trends

Temporal trends in the consumption of quinolone antibacterials (ATC group J01M) are presented in Table 3.11. Among countries reporting data for the period 2008–2012, community consumption of quinolone antibacterials (ATC group J01M) increased significantly in three countries (Belgium, Norway and Spain), while six countries (the Czech Republic, Cyprus, the Netherlands, Portugal, Sweden and the United Kingdom) showed a significant decrease in consumption of this group. The EU/EEA population-weighted mean quinolone consumption did not change significantly. Belgium, Norway and Spain showed a significant increase in the consumption of fluoroquinolones (ATC group J01MA), as did the EU/EEA population-weighted mean. The Czech Republic, Cyprus, the Netherlands, Sweden and the United Kingdom showed a significant decrease during the period 2008–2012.

Table 3.11. Trends of consumption of quinolone antibacterials (ATC group J01M) in the community, EU/EEA countries, 2008–2012, expressed as DDD per 1 000 inhabitants and per day

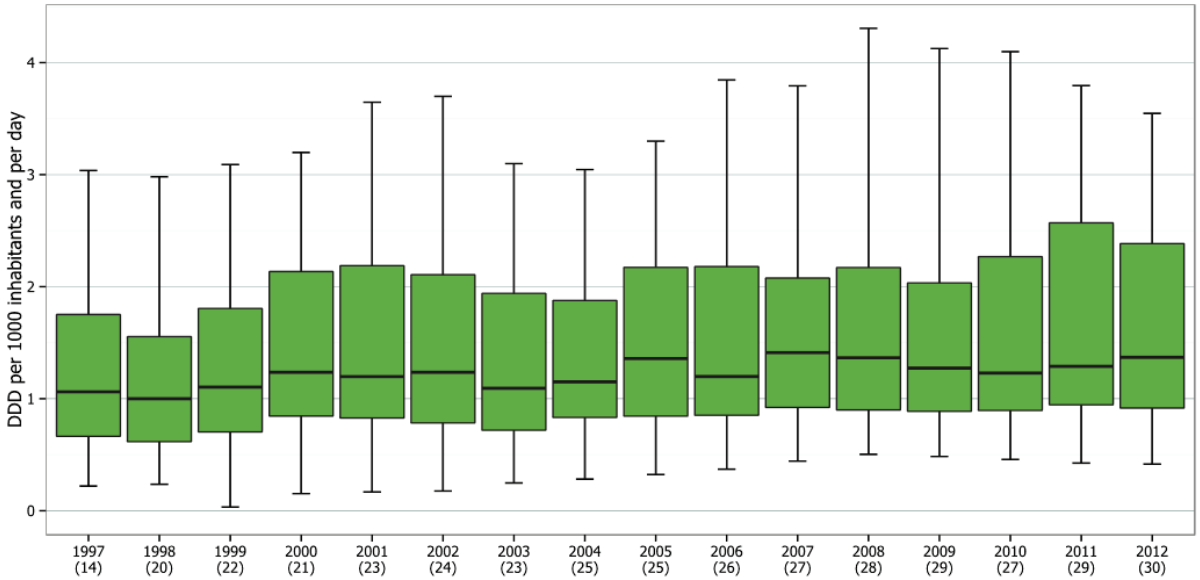
Country	2008	2009	2010	2011	2012	Trends in antimicrobial consumption, 2008–2012	Average annual change 2008–2012	Statistical significance
United Kingdom	0.5	0.5	0.5	0.4	0.4		-0.03	significant
Denmark	0.5	0.5	0.5	0.6	0.6		0.01	n.s.
Norway	0.5	0.5	0.5	0.6	0.6		0.02	significant
Sweden	0.8	0.8	0.8	0.8	0.7		-0.02	significant
Netherlands	0.9	0.9	0.9	0.8	0.8		-0.02	significant
Estonia	0.9	0.8	0.8	0.8	0.8		<0.01	n.s.
Ireland	1.0	0.9	0.9	0.9	0.9		-0.03	n.s.
Finland	0.8	0.9	0.9	0.9	0.9		0.02	n.s.
Lithuania	1.6*	1.2*	1.1*	1.2*	1.0			n.a.
Iceland	0.8	0.6	1.0*	1.1*	1.0*			n.a.
Latvia	1.0	0.9	0.9	1.0	1.0		0.01	n.s.
Czech Republic	1.2	1.3	1.2	1.1	1.1		-0.05	significant
Slovenia	1.1	1.1	1.1	1.1	1.1		-0.01	n.s.
Poland (c)	1.2	1.2	1.2	1.2	1.2			n.a.
Austria	1.3	1.3	1.4	1.3	1.3		-0.01	n.s.
Germany	1.4	1.5	1.5	1.5	1.4		0.01	n.s.
Croatia (a)					1.5			n.a.
EU/EEA	**1.8**	**1.8**	**1.8**	**1.8**	**1.8**		**0.01**	**n.s.**
Hungary (c)	1.8	1.8	2.0	1.9	1.9			n.a.
France	2.1	2.0	2.0	1.8	1.9		-0.05	n.s.
Slovakia (a)	1.9	2.0		2.5*	2.0			n.a.
Malta	1.8	1.7	1.8	1.9	2.0		0.07	n.s.
Greece	3.1*	2.6	2.9*	2.6	2.3			n.a.
Bulgaria	2.1	2.0	2.0	2.3	2.4		0.09	n.s.
Portugal	3.1	3.0	3.0	2.7	2.5		-0.15	significant
Spain (b)	2.4	2.4	2.5	2.6	2.6		0.05	significant
Belgium	2.4	2.6	2.7	2.7	2.8		0.08	significant
Luxembourg	2.8	2.8	2.9	2.8	2.8		0.01	n.s.
Romania (a)(b)(c)		1.3		3.4*	3.4*			n.a.
Italy	3.4	3.6	3.4	3.5	3.4		-0.01	n.s.
Cyprus	4.3*	4.1*	4.1*	3.8*	3.5*		-0.18	significant

**Total care data; including the hospital sector.*
(a) Croatia (2008–2011), Romania (2008 and 2010) and Slovakia (2010) did not report data for these years.
(b) Spain (2008–2012) and Romania (2009) reported reimbursement data, i.e. not including consumption without a prescription and other non-reimbursed courses.
(c) Hungary, Poland and Romania changed the type of data reported between 2008 and 2012 (reimbursement versus sales data).
EU/EEA refers to the corresponding population-weighted mean consumption.
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 2008 and 2012.
n.s.: not significant.

Additionally, six countries (France, Germany, Italy, the Netherlands, Slovenia, and Spain) and the EU/EEA population-weighted mean showed a significant decrease in the consumption of other quinolones (ATC group J01MB).

As shown in Figure 3.20, the median consumption of quinolone antibacterials (ATC group J01M) increased from 1.1 DDD per 1 000 inhabitants and per day in 1997 to 1.4 DDD per 1 000 inhabitants and per day in 2007 and has remained since then at a similar level.

Figure 3.20. Trends and inter-country variations of consumption of quinolone antibacterials (ATC group J01M) in the community, EU/EEA countries, 1997–2012, expressed as DDD per 1 000 inhabitants and per day



Boxes indicate the lower and the upper quartiles. The bold lines indicate the medians. Whiskers indicate the minimum and maximum values. For 1997-2009, only data from ESAC participating countries that also participated in ESAC-Net in 2012 are included. The number of participating countries is shown in parentheses.

Discussion

Fluoroquinolones, mostly ciprofloxacin (J01MA02), made up almost the entire consumption of quinolone antibacterials (ATC group J01M).

Over the period 2008–2012, one fifth of the countries showed a significant decrease in the consumption of fluoroquinolones (ATC group J01MA) in the community.

The total quinolone consumption in the community, as well as seasonal variation of this consumption, increased significantly between 1997 and 2009 [7]. During the same period, the ratio of third-generation to second-generation quinolone consumption also increased. However, the EU/EEA population-weighted mean consumption of quinolone antibacterials (ATC group J01M) has not increased or decreased significantly since 2008.

The large inter-country variation in the consumption of quinolone antibacterials (ATC J01M) may indicate inappropriate use in some of the reporting countries. Quinolone consumption is included in two proposed quality indicators for consumption in the community (J01MA_%, J01M_SV, Table 3.15).

3.1.8 Other antibacterials (ATC group J01X)

Results

The pattern of community consumption of other antibacterials (ATC group J01X) shows a gradient from northern to southern Europe (Figure 3.21). In 2012, consumption varied widely, ranging from 0.0006 DDD per 1 000 inhabitants and per day (Bulgaria) to 3.3 DDD per 1 000 inhabitants and per day (Norway) (Tables 3.1, 3.12 and 3.13), with a mean consumption of 0.7 DDD per 1 000 inhabitants and per day. The proportion of consumption of other antibacterials (ATC group J01X) out of the total consumption of antibacterials for systemic use (ATC group J01) ranged from <0.01% (Bulgaria) to 19.4% (Norway).

Nitrofurantoin (J01XE01) and nifurtoinol (J01XE02) accounted for more than 90% of the consumption of ATC group J01X in eight countries (Belgium, Croatia, Lithuania, Luxembourg, Malta, the Netherlands, Slovenia and the United Kingdom). Poland reported consumption of furazidin, a nitrofurantoin analogue without an ATC code or DDD. As an indication, if we had applied a DDD similar to that for nitrofurantoin (J01XE01) to furazidin, consumption of ATC group J01X in Poland would have been 2.8 DDD per 1 000 inhabitants and per day.

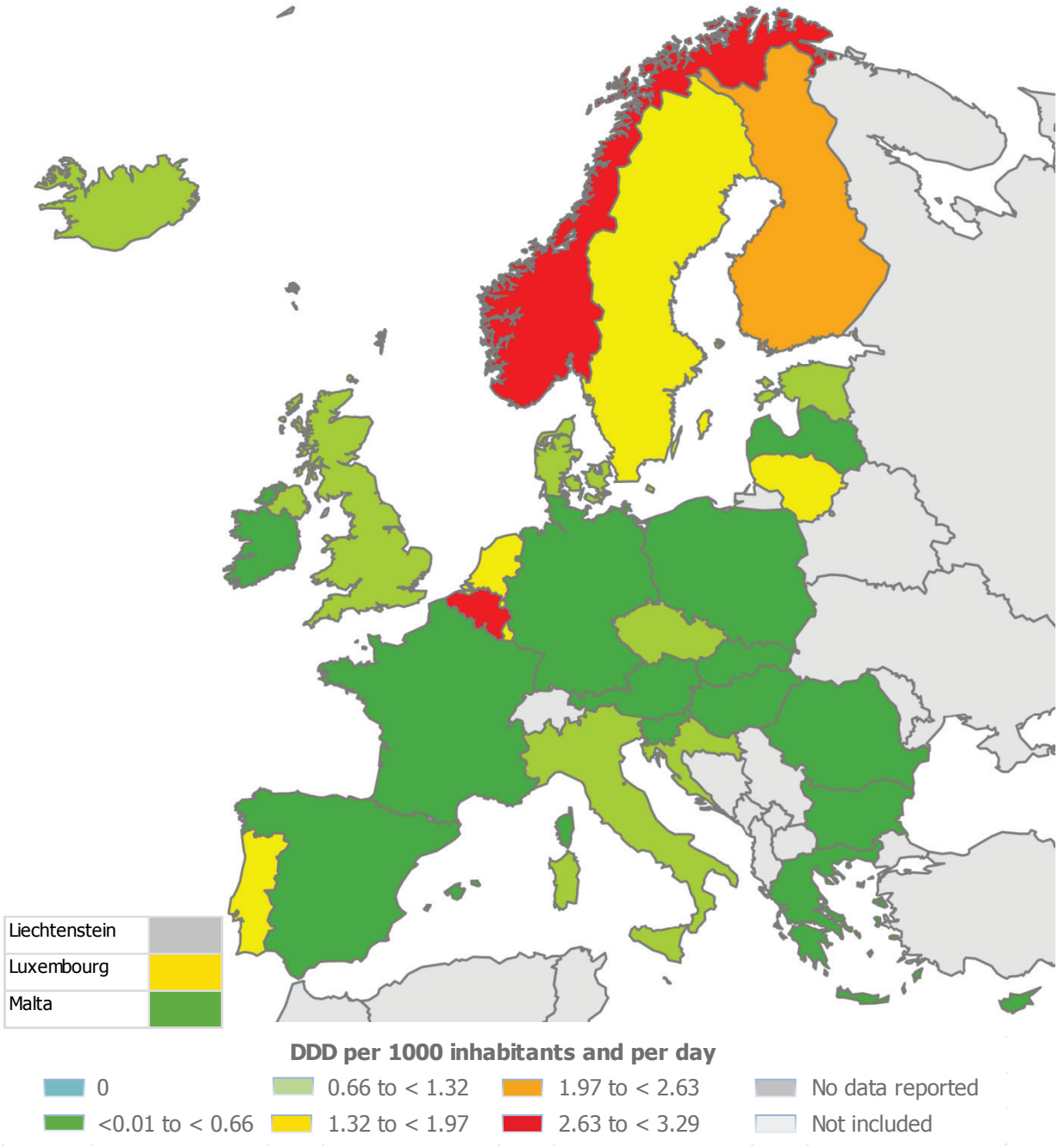
The Nordic countries showed the highest levels of consumption of methenamine (J01XX05), varying from 1.3 (Sweden) and 1.6 (Finland) DDD per 1 000 inhabitants and per day to 3.0 (Norway).

Table 3.12. Consumption of other antibacterials (ATC group J01X) at ATC group level 4 in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day

Country	Glycopeptide antibacterials (J01XA)	Polymyxins (J01XB)	Steroid antibacterials (J01XC)	Imidazole derivatives (J01XD)	Nitrofuran derivatives (J01XE)	Other antibacterials (J01XX)	Total (ATC group J01X)
Austria	<0.01	0.01	0.03	<0.01	0.21	0.03	0.28
Belgium	<0.01	0.02	0	0	2.48	0.15	2.64
Bulgaria	<0.01	0	0	0	0	<0.01	<0.01
Croatia	<0.01	0.00	0	0	0.68	<0.01	0.68
Cyprus (a)	0.04	0.01	0	0.09	0.34	0.02	0.50
Czech Republic	0.01	0.01	0	0.04	1.09	<0.01	1.15
Denmark	<0.01	0.02	0.01	<0.01	0.50	0.25	0.78
Estonia	<0.01	<0.01	<0.01	0.25	0.50	<0.01	0.75
Finland	<0.01	0	<0.01	<0.01	0.52	1.61	2.14
France	0	0.02	0.09	0	0.23	0.14	0.47
Germany	<0.01	0.01	0	<0.01	0.43	0.07	0.52
Greece	0.02	0.03	0.02	0.02	0.46	0.01	0.55
Hungary	<0.01	<0.01	0	<0.01	0.00	0.05	0.05
Iceland (a)	0.02	0	0	0.05	0.49	0.36	0.93
Ireland	<0.01	0.06	0.01	<0.01	0.00	0.01	0.08
Italy	<0.01	<0.01	0	<0.01	0.22	0.45	0.68
Latvia	<0.01	<0.01	0	0.01	0.21	0.04	0.26
Lithuania	<0.01	0	0	0.02	1.27	0.03	1.33
Luxembourg	<0.01	<0.01	0	<0.01	1.25	0.08	1.33
Malta	0	0	<0.01	0.04	0.31	0	0.34
Netherlands	<0.01	<0.01	<0.01	<0.01	1.38	0.05	1.43
Norway	<0.01	<0.01	<0.01	<0.01	0.32	2.96	3.29
Poland	<0.01	<0.01	0	<0.01	0*	<0.01	<0.01
Portugal	0	0	0.04	<0.01	1.21	0.18	1.44
Romania (a)	0.01	0.02	0	0.03	0.06	0.01	0.13
Slovakia	<0.01	0.01	0	<0.01	0	0.03	0.04
Slovenia	<0.01	<0.01	0	<0.01	0.11	<0.01	0.11
Spain (b)	<0.01	<0.01	0.01	<0.01	0.12	0.31	0.44
Sweden	<0.01	<0.01	0.01	<0.01	0.35	1.26	1.62
United Kingdom	<0.01	0.06	0.01	<0.01	0.79	0.02	0.88
EU/EEA mean (population-weighted)	**<0.01**	**0.01**	**0.02**	**<0.01**	**0.43**	**0.20**	**0.67**

(a) Cyprus, Iceland 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.
** Poland reported consumption of furazidin, a nitrofurantoin analogue without an ATC code or DDD.*

Figure 3.21. Consumption of other antibacterials (ATC group J01X) in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day



Cyprus, Iceland and Romania provided total care data, i.e. including the hospital sector.
Spain provided reimbursement data, i.e. not including consumption without a prescription or other non-reimbursed courses.
For more information on the map scales, see Chapter2.3.

Trends

Temporal trends in the consumption of other antibacterials (ATC group J01X) are presented in Table 3.13. Among countries reporting data for the period 2008–2012, community consumption increased significantly in 12 countries (Austria, Belgium, the Czech Republic, Estonia, Germany, Luxembourg, Malta, the Netherlands, Norway, Portugal, Slovenia and Spain), while two other countries (Ireland and Sweden) showed a significant decrease in consumption for this group during the same period. The EU/EEA population-weighted mean consumption did not change significantly.

Table 3.13. Trends of consumption of other antibacterials (ATC group J01X) in the community, EU/EEA countries, 2008–2012, expressed as DDD per 1 000 inhabitants and per day

Country	2008	2009	2010	2011	2012	Trends in antimicrobial consumption, 2008–2012	Average annual change 2008–2012	Statistical significance
Bulgaria	0.004	0.003	0.004	0.004	<0.001		<0.01	n.s.
Poland (c)	0.004	1.438	2.155	0.401	0.003			n.a.
Slovakia (a)	0.025	0.036		0.410*	0.038			n.a.
Hungary (c)	0.285	0.139	0.096	0.045	0.049			n.a.
Ireland	0.133	0.113	0.101	0.095	0.082		-0.01	significant
Slovenia	0.001	0.001	0.008	0.065	0.114		0.03	significant
Romania (a)(b)(c)		0.021		0.121*	0.135*			n.a.
Latvia	0.327	0.274	0.250	0.241	0.265		-0.02	n.s.
Austria	0.184	0.201	0.238	0.246	0.281		0.02	significant
Malta	0.124	0.175	0.238	0.428	0.343		0.07	significant
Spain (b)	0.324	0.344	0.391	0.412	0.438		0.03	significant
France	0.537	0.559	0.568	0.516	0.469		-0.02	n.s.
Cyprus	0.381*	0.451*	0.482*	0.460*	0.503*		0.03	n.s.
Germany	0.385	0.405	0.430	0.483	0.517		0.03	significant
Greece	0.752*	0.375	2.984*	0.564	0.546			n.a.
Italy	0.660	0.674	0.665	0.663	0.665		<0.01	n.s.
EU/EEA	**0.569**	**0.678**	**0.900**	**0.678**	**0.666**		**0.02**	**n.s.**
Croatia (a)					0.682			n.a.
Estonia	0.505	0.478	0.702	0.723	0.753		0.07	significant
Denmark	0.511	0.529	0.813	0.798	0.784		0.08	n.s.
United Kingdom	0.413	0.516	0.960	0.792	0.882		0.12	n.s.
Iceland	0.478	0.759	1.032*	1.042*	0.928*			n.a.
Czech Republic	0.742	0.869	0.764	1.031	1.152		0.10	significant
Lithuania	2.521*	2.732*	1.984*	1.972*	1.326			n.a.
Luxembourg	1.109	1.230	1.238	1.386	1.331		0.06	significant
Netherlands	1.138	1.196	1.260	1.353	1.434		0.07	significant
Portugal	0.846	0.949	0.988	1.372	1.436		0.16	significant
Sweden	1.868	1.742	1.651	1.618	1.621		-0.06	significant
Finland	2.096	2.096	2.086	2.044	2.138		<0.01	n.s.
Belgium	2.362	2.469	2.537	2.607	2.640		0.07	significant
Norway	2.669	2.855	3.057	3.161	3.291		0.15	significant

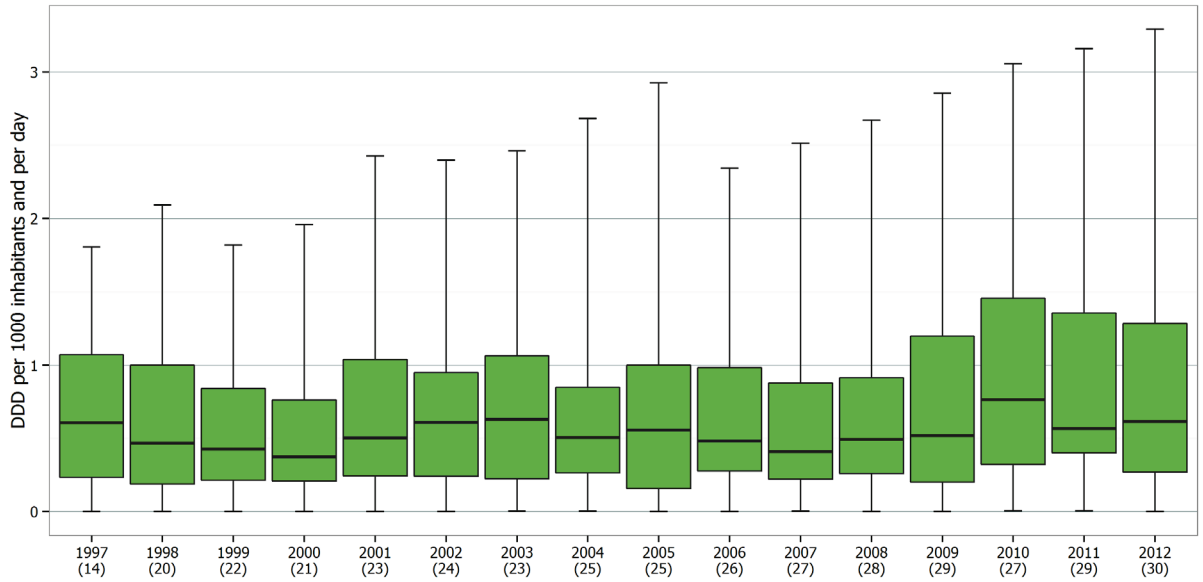
**Total care data; including the hospital sector.*
(a) Croatia (2008–2011), Romania (2008 and 2010) and Slovakia (2010) did not report data for these years.
(b) Spain (2008–2012) and Romania (2009) reported reimbursement data, i.e. not including consumption without a prescription or other non-reimbursed courses.
(c) Hungary, Poland and Romania changed the type of data reported between 2008 and 2012 (reimbursement versus sales data). EU/EEA refers to the corresponding population-weighted mean consumption;
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 2008 and 2012.
n.s.: not significant.

Additionally, significant trends over the five-year period (2008–2012) were observed for other antibacterials (ATC group J01X) at the fourth ATC level:

- Community consumption of parenteral glycopeptide antibacterials (ATC group J01XA) increased significantly in Cyprus. Four countries (Belgium, Italy, Norway and Sweden) showed a significant decrease. No significant change was observed for the EU/EEA population-weighted mean consumption.
- Community consumption of polymyxins (ATC group J01XB) increased significantly in five countries (Austria, Belgium, the Czech Republic, Germany and Italy). None of the countries showed a significant decrease. No significant change was observed for the EU/EEA population-weighted mean consumption.

- Community consumption of steroid antibacterials (ATC group J01XC) did not increase significantly in any country, whereas ten countries (Cyprus, Denmark, Finland, France, Ireland, Luxembourg, Portugal, Spain, Sweden and the United Kingdom) and the EU/EEA population-weighted mean showed a significant decrease in the consumption of this group.
- Community consumption of parenteral imidazole derivatives (ATC group J01XD) increased significantly in two countries (Germany and Italy), whereas no country showed a significant decrease in the consumption of this group. No significant change was observed for the EU/EEA population-weighted mean consumption.
- Community consumption of nitrofuran derivatives (ATC group J01XE) increased significantly in 12 countries (Austria, Belgium, Cyprus, Germany, Luxembourg, Malta, the Netherlands, Portugal, Slovenia, Spain, Sweden and the United Kingdom), whereas no country showed a significant decrease in the consumption of this group. No significant change was observed for the EU/EEA population-weighted mean consumption.
- Community consumption of other antibacterials (ATC group J01XX) increased significantly in 12 countries (Austria, Belgium, Finland, France, Germany, Luxembourg, the Netherlands, Norway, Poland, Portugal, Spain and the United Kingdom), whereas two countries (Latvia and Sweden) showed a significant decrease in the consumption of this group. No significant change was observed for the EU/EEA population-weighted mean consumption.

Figure 3.22 Trends and inter-country variations of consumption of other antibacterials (ATC group J01X) in the community, EU/EEA countries, 1997–2012, expressed as DDD per 1 000 inhabitants and per day



Boxes indicate the lower and the upper quartiles. The bold lines indicate the medians. Whiskers indicate the minimum and maximum values. For 1997-2009, only data from ESAC participating countries that also participated in ESAC-Net in 2012 are included. The number of participating countries is shown in parentheses.

Discussion

Over the five-year period 2008–2012, half of the countries included in the trend analyses showed a significant increase in consumption of other antibacterials (ATC group J01X). The overall increase was mainly due to an increased use of nitrofuran derivatives (ATC group J01XE) and of other antibacterials (ATC group J01XX) including those such as fosfomycin (J01XX01), methenamine (J01XX05) and linezolid (J01XX08).

The high consumption of methenamine reported for the Nordic countries, e.g. 3.3 DDD per 1 000 inhabitants and per year in Norway, is affected by the long duration of treatment for methenamine compared to shorter treatments for other antibacterials of ATC group J01X.

Although community parenteral consumption of glycopeptide antibacterials (ATC group J01XA), fosfomycin (J01XX01) and linezolid (J01XX08) is low, these trends are important since these antibacterials are mainly indicated for use to treat infections with multidrug-resistant bacteria, often in the hospital sector.

3.2 Consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01BA)

Results

In 2012, 25 countries reported data on consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01BA) in the community (Table 3.14 and Figure 3.23).

The consumption varied by a factor of 7.2 ranging from 0.46 DDD per 1 000 inhabitants and per day (Malta) to 3.32 DDD per 1 000 inhabitants and per day (Belgium). The EU/EEA population-weighted mean consumption was 1.24 DDD per 1 000 inhabitants and per day.

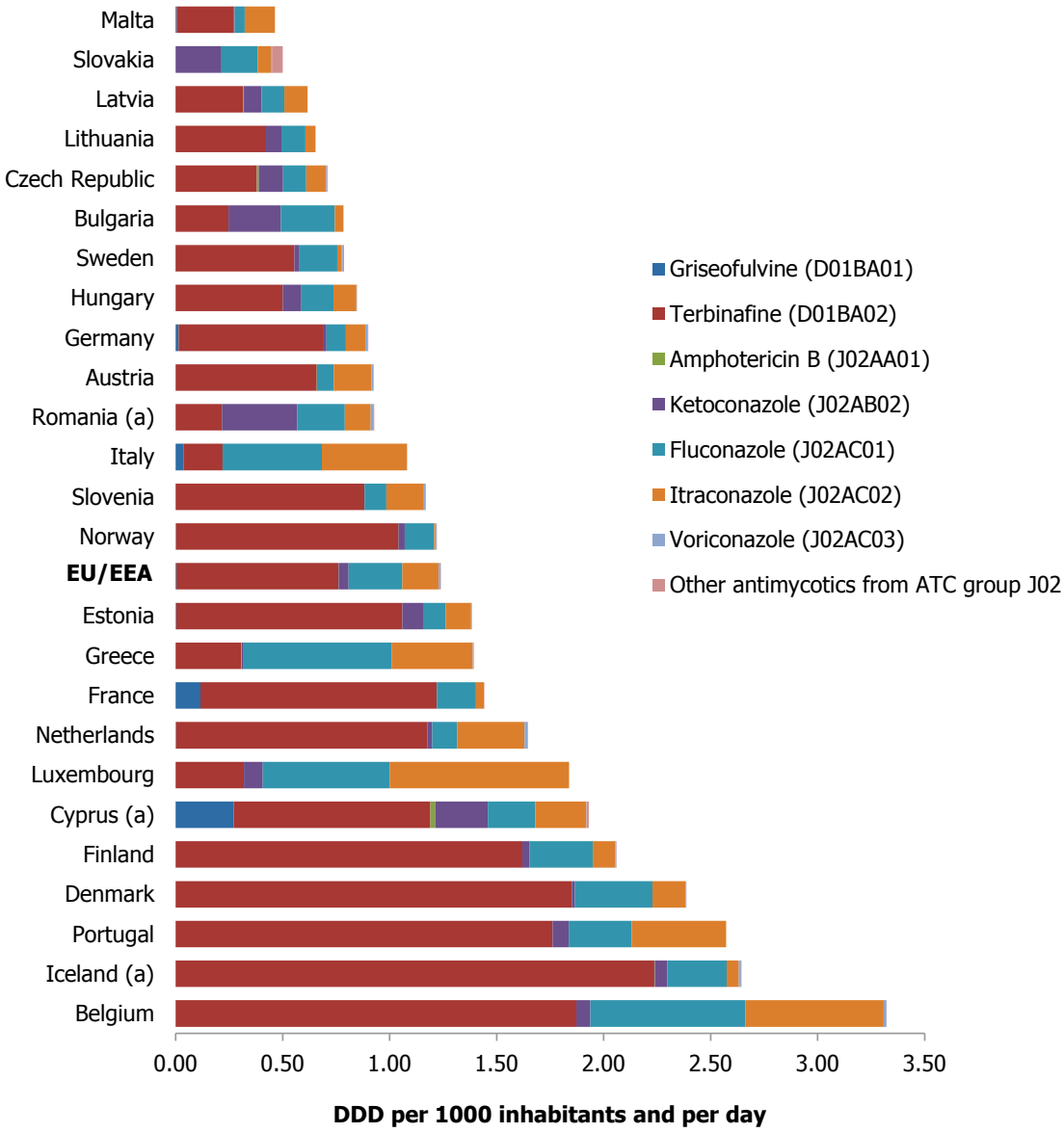
In 2012, terbinafine (D01BA02), ketoconazole (J02AB02), fluconazole (J02C01), and itraconazole (J02AC02) made up 98% of the total consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01BA) in the community in all countries.

Table 3.14. Consumption of antimycotics (ATC group J02) and antifungals (ATC group D01BA) for systemic use in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day

Country	Griseofulvine (D01BA01)	Terbinafine (D01BA02)	Amphotericin B (J02AA01)	Ketoconazole (J02AB02)	Fluconazole (J02AC01)	Itraconazole (J02AC02)	Voriconazole (J02AC03)	Other antimycotics for systemic use	Total (J02 & D01BA)
Austria	0	0.66	<0.01	0	0.08	0.18	0.01	<0.01	0.93
Belgium	0	1.87	0	0.07	0.72	0.65	0.01	<0.01	3.32
Bulgaria	0	0.25	0	0.24	0.25	0.04	<0.01	0	0.78
Cyprus (a)	0.27	0.92	0.02	0.25	0.22	0.24	<0.01	0.01	1.93
Czech Republic	0	0.38	0.01	0.11	0.11	0.09	0.01	<0.01	0.71
Denmark	0	1.85	<0.01	0.01	0.36	0.15	<0.01	0	2.39
Estonia	<0.01	1.06	0	0.10	0.11	0.12	<0.01	0	1.38
Finland	0	1.62	<0.01	0.03	0.30	0.10	0.01	<0.01	2.06
France	0.12	1.11	0	0	0.18	0.04	0	<0.01	1.44
Germany	0.01	0.68	<0.01	0.01	0.09	0.09	0.01	<0.01	0.90
Greece	0	0.31	<0.01	0.01	0.69	0.38	<0.01	<0.01	1.39
Hungary	0	0.50	0	0.09	0.15	0.11	<0.01	<0.01	0.85
Iceland (a)	0	2.24	<0.01	0.06	0.28	0.06	0.01	<0.01	2.64
Italy	0.04	0.18	0	0	0.46	0.40	0	<0.01	1.08
Latvia	<0.01	0.32	<0.01	0.08	0.11	0.11	0	0	0.62
Lithuania	0	0.42	0	0.07	0.11	0.05	<0.01	<0.01	0.65
Luxembourg	0	0.32	0	0.09	0.59	0.84	0	0	1.84
Malta	0.01	0.27	0	<0.01	0.05	0.14	0	0	0.46
Netherlands	<0.01	1.17	<0.01	0.02	0.12	0.32	0.01	<0.01	1.65
Norway	<0.01	1.04	<0.01	0.03	0.14	0.01	<0.01	<0.01	1.22
Portugal	0	1.76	0	0.08	0.30	0.44	0	0	2.57
Romania (a)	0	0.22	<0.01	0.35	0.22	0.12	0.01	<0.01	0.93
Slovakia	0	0	0	0.21	0.17	0.06	0.01	0.05	0.50
Slovenia	0	0.88	0	0	0.10	0.17	0.01	<0.01	1.17
Sweden	<0.01	0.55	0	0.02	0.18	0.02	0.01	<0.01	0.79
EU/EEA mean (population-weighted)	**<0.01**	**0.76**	**<0.01**	**0.05**	**0.25**	**0.17**	**0.01**	**<0.00**	**1.24**

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

Figure 3.23. Consumption of antifungals (ATC group D01BA) and antimycotics (ATC group J02) for systemic use in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day



(a) Cyprus, Iceland and Romania provided total care data, i.e. including the hospital sector.
EU/EEA refers to the corresponding population-weighted mean consumption based on 25 countries that provided data.

Terbinafine (D01BA02) consumption alone accounted for more than 50% of the total consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01BA) in 18 (72%) of the reporting countries. The proportion of terbinafine consumption ranged from 17.0% (Italy) to 85.0% (Norway).

In the Netherlands and in Denmark, countries that generally have a low consumption of antibacterials for systemic use (ATC group J01), the total consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01BA) was 1.3 and 1.9 times higher, respectively, than the EU/EEA population-weighted mean total consumption (1.3 DDD per 1 000 inhabitants and per day). EU/EEA refers to the corresponding population-weighted mean consumption based on the 25 countries that provided data.

Trends

The analysis of trends in the community consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01BA) during 2008–2012 included 19 countries and only showed a significant increase for Finland and Norway (see also Chapter 2.3 for trend analyses). Three countries (Austria, the Czech Republic and France)

showed a significant decrease in the consumption of this group; no significant change for the EU/EEA population-weighted mean consumption was observed.

Discussion

Of all 14 substances under surveillance (12 antimycotics of ATC group J02 and two antifungals of ATC group D01BA), four substances dominated the consumption patterns as in previous years.

Seasonal variations of the consumption of antifungals and antimycotics for systemic use have previously been described [15]. Such variations were not analysed for this report. Similar to antibacterials for systemic use, the fact that six countries (Austria, Belgium, the Czech Republic, Germany, Luxembourg and Romania) reported reimbursement data may have resulted in underreporting as data on antifungals and antimycotics that were obtained without prescription or not reimbursed because the price was below a reimbursement limit, are not included in reimbursement databases [11, 15].

Nevertheless, ESAC-Net data and historical data from the ESAC project are publicly available, standardised and validated European reference data on consumption of antifungals and antimycotics for systemic use (ATC groups J02 & D01BA). These data can be used for monitoring and evaluating policies for appropriate prescribing in the community [15].

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

Background

In 2007, the ESAC project published antimicrobial consumption data in the community in Europe by adopting 12 consensus quality indicators based on ESAC project data from 1997 to 2003. It was concluded that these indicators could be used to better describe antimicrobial consumption and to assess changes in national prescribing patterns in Europe, and that work towards improvement of indicator values could have an impact on reducing antimicrobial resistance, improving patient health benefit and cost-effectiveness and provide information for public health policy makers [2]. The consumption data are presented by adopting these quality indicators grouped as follows:

- Total consumption of antibacterials for systemic use (ATC group J01) and subgroups;
- Relative consumption of beta-lactamase-sensitive penicillins, combinations of penicillins including beta-lactamase inhibitors, third- and fourth-generation cephalosporins, and fluoroquinolones;
- The ratio of broad- to narrow-spectrum antibacterials;
- Seasonal variations of total consumption of antibacterials for systemic use and of consumption of quinolone antibacterials.

Results

The values of the proposed quality indicators for the 30 reporting countries in 2012 are presented in Table 3.15. In addition, the minimum value (p0), 25th percentile (p25), median (p50), 75th percentile (p75) and maximum value (p100) are displayed at the bottom of the table. For all quality indicators except J01CE_%, low values of the indicator suggest better quality with the best quality being within the first quartile (i.e. p0 ≤ values ≤ p25). For the indicator J01CE_%, high values of the indicator suggest better quality with the best quality being within the fourth quartile (i.e. p75 < values ≤ p100).

Quality indicators on total consumption of antibacterials for systemic use (ATC group J01) and subgroups

The first five indicators (displayed as J01, J01C, J01D, J01F and J01M) report consumption expressed in DDD per 1 000 inhabitants and per day for ATC group J01 and four subgroups (ATC J01C, J01D, J01F and J01M). The values correspond to the results presented in Chapter 3 (Table 3.1 and Figure 3.1).

The Netherlands reported values within the first quartile (p0-p25) for all five indicators. Latvia and Sweden reported values within the first quartile for ATC group J01 and for three other indicators. Conversely, Luxembourg reported values within the fourth quartile (p75-p100) for all five indicators.

Quality indicators on the relative consumption of beta-lactamase-sensitive penicillins, combinations of penicillins including beta-lactamase inhibitors, third- and fourth-generation cephalosporins, and fluoroquinolones

The next four indicators (displayed as J01CE_%, J01CR_%, J01DD+DE_% and J01MA_%) report on the percentage of the total consumption of antibacterials for systemic use (ATC group J01) corresponding to various subgroups: beta-lactamase-sensitive penicillins (ATC group J01CE), combinations of penicillins including beta-lactamase inhibitors (ATC group J01CR), third- and fourth-generation cephalosporins (ATC groups J01DD and J01DE), and fluoroquinolones (ATC group J01MA).

- Three countries (Denmark, Finland and Norway) reported values within the quartiles suggesting the best quality for all four indicators (see above under Results).
- Conversely, Italy reported values within the quartiles suggesting the lowest quality for all four indicators.
- Indicator J01CE_% (relative consumption of beta-lactamase-sensitive penicillins) ranged from <0.1% to 27.9%. The Czech Republic, Denmark, Finland, Iceland, Norway, Slovenia and Sweden reported values within the fourth quartile, suggesting a better quality than all other quartiles.
- Indicator J01CR_% (relative consumption of combinations of penicillins including beta-lactamase inhibitors) ranged from <0.1% to 41.1%. Denmark, Finland, Germany, Latvia, Lithuania, Norway, Sweden and the United Kingdom showed values within the first quartile suggesting a better quality than all other quartiles.
- Indicator J01DD+DE_% (relative consumption of third- and fourth-generation cephalosporins) ranged from <0.1% to 6.8%. Belgium, Denmark, Estonia, Finland, Lithuania, Luxembourg, the Netherlands, Norway, Poland and the United Kingdom showed values within the first quartile, suggesting a better quality than all other quartiles.
- Indicator J01MA_% (relative consumption of fluoroquinolones) ranged from 2.1% to 13.7%. Denmark, Finland, Iceland, Ireland, Lithuania, Norway, Sweden and the United Kingdom showed values within the first quartile suggesting a better quality than all other quartiles.

Quality indicator on the ratio of broad- to narrow-spectrum antibacterials

The tenth quality indicator as defined in [2] and displayed as J01_B/N reports on the ratio of the consumption of broad-spectrum penicillins, cephalosporins and macrolides to the consumption of narrow-spectrum penicillins, cephalosporins and macrolides. The indicator values ranged from 0.2% in Sweden to 258.3% in Greece.

Quality indicators on seasonal variations of total consumption of antibacterials for systemic use and of consumption of quinolone antibacterials

The last two quality indicators (displayed as J01_SV and J01M_SV) report on seasonal variations of the total consumption of antibacterials for systemic use (ATC group J01) and of consumption of quinolone antibacterials (J01M). As these indicators are calculated based on consecutive winter quarters and summer quarters they start in July prior to the year of data reporting for the current report (the period for calculating seasonal variations for this report starts in July 2011) and ending one year later (i.e. in June 2012). These indicators could only be calculated for the 12 countries that provided quarterly data for the year of the third ESAC-Net report (2012 consumption data) and the year before (see legend of Table 3.15).

Indicator values for the seasonality of total consumption of antibacterials for systemic use (ATC group J01) ranged from 11.7% (United Kingdom) to 55.0% (Hungary).

The indicator values for seasonality of the consumption of quinolone antibacterials (J01M) ranged from 0.4% (United Kingdom) to 32.9% (Hungary).

Trends

Among countries reporting data for the period 2008–2012, trends for the first five quality indicators expressed in DDD per 1 000 inhabitants and per day for ATC group J01 and four subgroups (ATC J01C, J01D, J01F and J01M) are shown in the corresponding chapters (Chapters 3.1, 3.1.3, 3.1.4, 3.1.6 and 3.1.7).

Additionally, trends were assessed for the four indicators which report on the percentage of the total consumption of antibacterials for systemic use (ATC group J01) corresponding to the following subgroups: beta-lactamase-sensitive penicillins (displayed as J01CE_%), combinations of penicillins including beta-lactamase inhibitors (displayed as J01CR_%), third- and fourth-generation cephalosporins (displayed as J01DD+DE_%), and fluoroquinolones (displayed as J01MA_%).

Ireland reported a significant increase for the indicator J01CE_%. A significant decrease for this indicator was observed in 11 countries (Austria, Belgium, Bulgaria, Denmark, Estonia, Italy, Latvia, Luxembourg, the Netherlands, Norway and Spain).

Conversely, a significant increase for the indicator J01CR_% was observed in ten countries (Austria, Denmark, Estonia, France, Germany, Ireland, Italy, Luxembourg, Slovenia and the United Kingdom). No country showed a significant decrease of this indicator.

A significant increase of the indicator J01DD+DE_% was observed in three countries (Belgium, Estonia and Malta). A significant decrease was observed in six countries (Austria, Bulgaria, Ireland, Slovenia, Spain and the United Kingdom).

A significant increase of the indicator J01MA_% was observed in Bulgaria. A significant decrease was observed in six countries (the Czech Republic, Ireland, the Netherlands, Portugal, Sweden and the United Kingdom).

Discussion

In half of the EU/EEA countries which were included in the trend analysis, trends of the results used for quality indicators J01CE_% and J01CR_% confirmed a significant decrease in the consumption of beta-lactamase-sensitive penicillins (ATC group J01CE) and a significant increase of the consumption of the broad-spectrum combinations of penicillins, including beta-lactamase inhibitors (ATC group J01CR). Conversely, trends in the proportion of third- and fourth-generation cephalosporins and of fluoroquinolones did not show a clear increasing or decreasing trend.

Table 3.15. ESAC quality indicators for consumption data of antibacterials for systemic use (ATC group J01) from the community, EU/EEA countries, 2012

(The indicator codes are explained in the legend)

	Consumption (DDD per 1000 inhabitants and per day)					Relative consumption (%)				Broad/ narrow	Seasonal variation	
Country	J01*	J01C	J01D	J01F	J01M	J01CE_ % ǂ	J01CR_ %	J01DD +DE_ %	J01MA _%	J01_B/ N	J01_SV	J01M_SV
Austria	13.93	6.29	1.58	3.18	1.29	5.8	32.0	4.1	9.3	8.09	29.4	18.0
Belgium	29.76	17.02	1.53	3.39	2.76	0.1	30.3	<0.1	9.3	79.17	33.4	26.1
Bulgaria	18.47	7.79	2.44	3.05	2.40	1.3	13.7	2.3	13.0	10.07	-	-
Croatia	21.72	11.19	3.53	2.97	1.49	3.8	35.1	3.6	6.9	8.15	-	-
Cyprus (a)	29.71	13.85	5.37	2.92	3.55	0.3	30.7	2.4	11.9	28.45	-	-
Czech Republic	17.54	7.05	1.44	3.48	1.06	8.4	21.6	0.4	6.0	5.43	17.3	9.1
Denmark	16.43	10.26	0.03	2.25	0.55	27.9	6.4	<0.1	3.4	0.59	16.1	6.2
Estonia	11.61	4.42	0.98	2.43	0.84	1.9	13.3	<0.1	7.3	10.54	29.9	8.4
Finland	19.46	6.48	2.30	1.55	0.89	6.8	7.4	<0.1	4.6	0.82	21.0	10.9
France	29.68	17.41	2.39	3.70	1.92	0.5	24.5	5.6	6.3	50.63	-	-
Germany	14.87	4.48	2.82	2.68	1.45	5.7	2.6	3.0	9.7	4.94	31.2	25.5
Greece	31.92	12.67	6.45	7.67	2.33	0.1	18.9	0.2	7.3	258.32	-	-
Hungary	13.76	6.30	1.75	2.40	1.91	2.7	32.9	2.5	13.7	21.49	55.0	32.9
Iceland (a)	22.11	12.04	0.70	1.66	1.02	11.0	17.5	0.3	4.6	1.68	16.1	8.4
Ireland	23.02	12.53	1.24	4.17	0.87	4.3	29.6	0.4	3.8	6.46	17.4	14.2
Italy	27.56	15.36	2.37	4.69	3.48	<0.1	39.8	6.8	12.2	158.44	34.3	23.9
Latvia	13.06	6.24	0.47	1.53	1.03	0.1	13.0	0.3	7.6	11.50	-	-
Lithuania	16.17	9.11	0.92	1.88	1.00	1.1	10.6	0.1	5.9	10.54	-	-
Luxembourg	27.86	13.82	3.65	4.04	2.79	0.1	32.6	0.1	10.0	47.47	35.3	21.0
Malta	22.48	8.99	5.27	3.70	2.01	0.2	35.6	1.3	8.9	162.07	-	-
Netherlands	11.34	4.50	0.04	1.50	0.81	3.0	16.0	0.1	7.1	7.82	-	-
Norway	16.92	6.83	0.11	2.00	0.56	21.2	<0.1	<0.1	3.3	0.23	-	-
Poland	19.79	9.07	2.17	3.48	1.19	0.8	19.3	0.1	6.0	36.93	-	-
Portugal	22.66	12.38	1.55	3.21	2.47	0.1	41.1	1.0	10.9	34.85	23.1	6.7
Romania (a)	30.40	17.19	4.36	2.67	3.38	3.3	25.6	3.0	11.1	8.39	-	-
Slovakia	20.02	7.91	3.49	4.91	1.95	6.5	23.9	2.6	9.8	8.85	-	-
Slovenia	14.30	9.62	0.30	1.80	1.08	13.6	29.3	0.5	7.6	3.22	30.2	9.7
Spain (b)	20.87	13.11	1.52	1.98	2.61	0.4	38.5	2.2	12.3	66.34	-	-
Sweden	14.07	7.01	0.18	0.63	0.75	27.7	1.7	0.2	5.3	0.17	-	-
United Kingdom	20.06	9.33	0.35	3.10	0.42	4.0	6.6	<0.1	2.1	1.35	11.7	0.4
p0	11.34	4.42	0.03	0.63	0.42	0.0	0.02	0.0	2.08	0.17	11.67	0.41
p25	15.20	6.87	0.75	1.98	0.92	0.3	13.12	0.1	5.91	5.06	17.33	8.40
p50	19.91	9.22	1.56	2.94	1.37	2.8	22.76	0.4	7.44	9.46	29.37	10.93
p75	22.93	12.63	2.72	3.48	2.39	6.5	31.66	2.4	9.96	36.41	32.32	22.50
p100	31.92	17.41	6.45	7.67	3.55	27.9	41.12	6.8	13.75	258.32	55.01	32.92

** Denominator for relative consumption; ǂ Indicators within the fourth quartile (i.e. values > percentile 75 (p75) suggest better quality than indicator values within the third quartile (i.e. p50 ≤ values < p75) and so on.*

(a) Cyprus, Iceland 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 or other non-reimbursed courses.

*Definitions of indicator codes***

Indicators on consumption of antibacterials for systemic use (ATC group J01) and at ATC group level 3:

J01	J01_DID	Consumption of antibacterials for systemic use (J01) expressed in DDD per 1000 inhabitants and per day
J01C	J01C_DID	Consumption of penicillins (J01C) expressed in DDD per 1000 inhabitants and per day
J01D	J01D_DID	Consumption of cephalosporins (J01D) expressed in DDD per 1000 inhabitants and per day
J01F	J01F_DID	Consumption of macrolides, lincosamides and streptogramins (J01F) expressed in DDD per 1000 inhabitants and per day
J01M	J01M_DID	Consumption of quinolones (J01M) expressed in DDD per 1000 inhabitants and per day

Indicators on the relative consumption of antibacterials for systemic use (ATC group 3):

J01CE_%	J01CE_%	Consumption of beta-lactamase-sensitive penicillins (J01CE) expressed as percentage of the total consumption of antibacterials for systemic use (J01)
J01CR_%	J01CR_%	Consumption of combination of penicillins, including beta-lactamase inhibitor (J01CR) expressed as percentage of the total consumption of antibacterials for systemic use (J01)
J01DD+DE_%	J01DD+DE_%	Consumption of third- and fourth-generation cephalosporins (J01(DD+DE)) expressed as percentage of the total consumption of antibacterials for systemic use (J01)
J01MA_%	J01MA_%	Consumption of fluoroquinolones (J01MA) expressed as percentage of the total consumption of antibacterials for systemic use (J01)

Indicators on the ratio of broad and narrow spectrum antibacterials:

J01_B/N	J01_B/N	Ratio of the consumption of broad-spectrum penicillins, cephalosporins and macrolides (J01(CR+DC+DD+(F-FA01))) to the consumption of narrow-spectrum penicillins, cephalosporins and macrolides (J01(CE+DB+FA01))

Indicators on seasonal variation of antibacterials for systemic consumption (ATC group J01, subgroup J01M):

J01_SV	J01_SV	Seasonal variation of the total antibiotic consumption (J01) of a 12-month period starting in July and ending the following June, expressed as percentage: [(DDD (winter quarters)/DDD (summer quarters)-1] x 100
J01M_SV	J01M_SV	Seasonal variation of quinolone consumption (J01M) of a 12-month period starting in July and ending the following June, expressed as percentage: [(DDD (winter quarters)/DDD (summer quarters)-1] x 100

*** The second column shows the original labels of the quality indicators as described in the article 'European Surveillance of Antimicrobial Consumption (ESAC): quality indicators for outpatient antibiotic use in Europe' published in Qual Saf Health Care 2007;16:440–445.*

Any ranking of the countries 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 of the ratio of broad- to narrow-spectrum penicillins, cephalosporins and macrolides. For countries where changes in the ranking suggest quality improvement, this could just reflect a relative change compared to other countries, e.g. that quality decreased in all countries but less in that specific country [1]. It should be emphasised that these indicators cannot by themselves indicate quality of antimicrobial use unless they are utilised with corresponding clinical data (e.g. resistance pattern).

Finally, 2012 data for the three countries (Cyprus, Iceland and Romania) that reported only total care data, i.e. including hospital sector data, were included in Table 3.15 because the largest proportion of consumption of antibacterials for systemic use (ATC group J01) is reported from the community. However, quality indicators from these three countries should be interpreted with caution because certain antibacterials, e.g. broad-spectrum antibacterials, make up a larger proportion of total consumption in the hospital sector than in the community.

4 Consumption of antimicrobials for systemic use in the hospital sector

4.1 Consumption of antibacterials for systemic use (ATC group J01)

Results

For 2012, 20 countries reported data on consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, an increase from 10 in 1997. Table A2 (see Annexes) provides an overview of the total consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, reported for each country during the period 1997–2012.

In 2012, consumption of antibacterials for systemic use (ATC group J01) in the hospital sector varied from 1.0 (the Netherlands) to 2.8 (Finland) DDD per 1 000 inhabitants and per day with an EU/EEA population-weighted mean consumption of 2.0 DDD per 1 000 inhabitants and per day (Table 4.1).

Table 4.1 and Figure 4.1 present the consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, as a total and by subgroups.

Table 4.1. Consumption of antibacterials for systemic use (ATC group J01) by ATC group level 3 in the hospital sector, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day

Country	Tetra-cyclines (J01A)	Beta-lactams, penicillins (J01C)	Other beta-lactam antibac-terials (J01D)	Sulfonamides and trimethoprim (J01E)	Macrolides, lincosamides and strepto-gramins (J01F)	Quino-lones (J01M)	Other antibac-terials (J01X)	Sum (J01B, J01G, and J01R)*	Total (ATC group J01)
Belgium	0.02	0.87	0.35	0.02	0.08	0.21	0.12	0.03	1.71
Bulgaria	0.02	0.18	0.81	0.01	0.12	0.14	0.01	0.12	1.40
Croatia	0.06	0.65	0.57	0.06	0.16	0.22	0.15	0.11	1.98
Denmark	0.04	0.88	0.31	0.07	0.09	0.21	0.14	0.04	1.78
Estonia	0.09	0.65	0.54	0.05	0.22	0.31	0.16	0.07	2.09
Finland (a)	0.24	0.53	0.93	0.13	0.15	0.30	0.50	0.02	2.79
France	0.01	1.23	0.29	0.04	0.11	0.27	0.13	0.05	2.12
Greece	0.05	0.57	0.57	0.02	0.17	0.26	0.32	0.08	2.05
Ireland	0.03	0.87	0.16	0.07	0.26	0.13	0.18	0.07	1.76
Italy	0.02	0.88	0.44	0.04	0.20	0.44	0.38	0.06	2.46
Latvia	0.18	0.62	0.65	0.08	0.15	0.34	0.17	0.09	2.27
Lithuania	0.07	0.95	0.57	0.05	0.06	0.37	0.17	0.16	2.39
Luxembourg	0.01	0.71	0.66	0.03	0.16	0.26	0.12	0.05	2.00
Malta	0.07	0.47	0.26	0.03	0.21	0.23	0.11	0.06	1.44
Netherlands	0.02	0.43	0.18	0.03	0.07	0.12	0.07	0.04	0.96
Norway	0.06	0.66	0.33	0.04	0.08	0.09	0.13	0.06	1.44
Portugal (b)	0.01	0.51	0.44	0.06	0.16	0.09	0.11	0.08	1.46
Slovakia	0.02	0.81	0.53	0.03	0.10	0.29	0.17	0.06	2.02
Slovenia	0.01	0.67	0.33	0.05	0.12	0.23	0.10	0.05	1.56
Sweden	0.21	0.84	0.19	0.07	0.06	0.16	0.09	0.02	1.65
EU/EEA mean (population-weighted)	**0.04**	**0.87**	**0.39**	**0.04**	**0.14**	**0.28**	**0.20**	**0.06**	**2.01**

(a) Finland: data include consumption in remote primary healthcare centres and nursing homes.
(b) Portugal: data correspond to public hospitals only.
EU/EEA refers to the corresponding population-weighted mean consumption based on the 20 countries that provided data.
**J01B: amphenicols; J01G: aminoglycoside antibacterials; J01R: combinations of antibacterials*

The proportion of consumption of tetracyclines (ATC group J01A) out of the total consumption of antibacterials for systemic use (ATC group J01) ranged from 0.5% (France) to 12.8% (Sweden).

The proportion of consumption of penicillins (ATC group J01C) ranged from 12.5% (Bulgaria) to 58.2% (France). In three countries (Belgium, France and Sweden) the subgroup of penicillins with enzyme inhibitors (J01C) made up ≥50% of the total consumption of antibacterials for systematic use (ATC group J01).

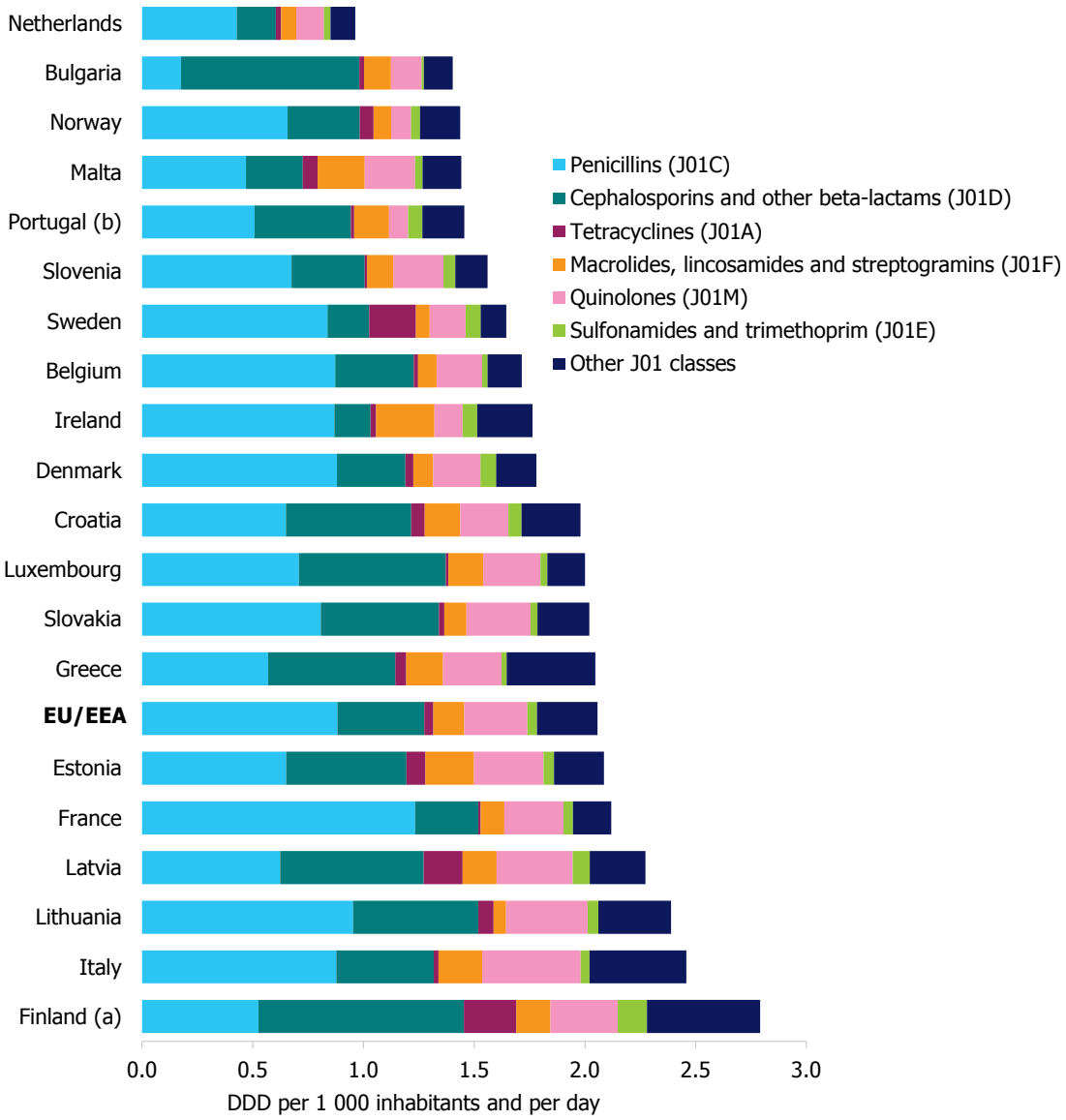
The proportion of consumption of cephalosporins and other beta-lactams (ATC group J01D) was the highest in Bulgaria (57.4%), and the lowest in Ireland (9.3%).

The proportion of consumption of sulfonamides and trimethoprim (ATC group J01E) ranged from 0.7% (Bulgaria) to 4.7% (Finland).

The proportion of consumption of macrolides, lincosamides and streptogramins (ATC group J01F) ranged from 2.4% (Lithuania) to 14.9% (Ireland).

The proportion of the consumption of quinolone antibacterials (ATC group J01M) ranged from 6.0% (Portugal) to 18.1% (Italy).

Figure 4.1. Consumption of antibacterials for systemic use (ATC group J01) in the hospital sector in EU/EEA countries, 2012, at group level 3, expressed as DDD per 1 000 inhabitants and per day



(a) Finland: data include consumption in remote primary healthcare centres and nursing homes.
(b) Portugal: data correspond to public hospitals only.
EU/EEA refers to the corresponding population-weighted mean consumption based on 20 countries that provided data.

In 2012, consumption of penicillins with enzyme inhibitors (ATC group J01CR) varied from 0.03 (Norway) to 0.8 (France) DDD per 1 000 inhabitants and per day with an EU/EEA population-weighted mean consumption of 0.6 DDD per 1 000 inhabitants and per day. Penicillins with enzyme inhibitors accounted for ≥75% of the consumption of penicillins (ATC group J01C) in seven countries (Bulgaria, Croatia, Italy, Luxembourg, Malta, Portugal and Slovakia).

In 2012, consumption of carbapenems (ATC group J01DH) varied by a factor of 14, from 0.01 (Bulgaria) to 0.14 DDD per 1 000 inhabitants and per day (Portugal). The proportion of consumption of carbapenems (ATC group J01DH) out of antibacterials for systemic use (ATC group J01) ranged from 0.8% (Latvia) to 9.8% (Portugal) with an EU/EEA population-weighted mean of 2.9%.

In 2012, consumption of glycopeptide antibacterials (ATC group J01XA) varied from 0.01 (Lithuania) to 0.08 (Greece) DDD per 1 000 inhabitants and per day. The proportion of consumption of glycopeptide antibacterials (ATC group J01XA) out of antibacterials for systemic use (ATC group J01) ranged from 0.5% (Lithuania) to 4.2% (Portugal) with an EU/EEA population-weighted mean of 2.2%.

Trends

Trends in the consumption of antibacterials for systemic use (ATC group J01) in the hospital sector from 2008 to 2012 are presented in Table 4.2 (see also Chapter 2.3 for trend analyses). Among the 11 countries reporting data for the period 2008–2012 and hence included in the trend analysis, only Bulgaria showed a significant decrease of consumption in the hospital sector for the whole group of antibacterials for systemic use (ATC group J01). The EU/EEA population-weighted mean consumption did not change significantly during the period.

Additionally, significant trends in consumption in the hospital sector over the five-year period (2008–2012) were observed for six sub-groups of antibacterials for systemic use (ATC group J01) and for three selected subgroups at the fourth ATC group level. For all these trends the EU/EEA population-weighted mean consumption is only mentioned when it significantly increased or decreased during the period.

- Consumption of tetracyclines (ATC group J01A) increased significantly in Ireland and Latvia, whereas none of the countries showed a significant decrease.
- Consumption of beta-lactams, penicillins (ATC group J01C) increased significantly in Sweden, whereas only one country (Bulgaria) showed a significant decrease. In the subgroup penicillins with enzyme inhibitors (J01CR), consumption increased significantly in four countries (Denmark, Estonia, Norway and Sweden), whereas no significant decrease was reported.
- Consumption of other beta-lactam antibacterials (ATC group J01D) significantly increased in Bulgaria while one country (Slovenia) showed a significant decrease. For the subgroup carbapenems (J01DH), consumption increased significantly in seven countries (Denmark, Estonia, France, Ireland, Norway, Slovenia and Sweden), as did the EU/EEA population-weighted mean. No significant decrease was reported.
- Consumption of sulfonamides and trimethoprim (ATC group J01E) did not change significantly in any country included in the trend analysis for the period 2008–2012.
- Consumption of macrolides, lincosamides and streptogramins (ATC group J01F) changed significantly only in two countries: Latvia reported a significant increase and Slovenia a significant decrease in consumption.
- Consumption of quinolone antibacterials (ATC group J01M) did not significantly increase in any country included in the trend analysis for the period 2008–2012. Two countries (Denmark and Norway) showed a significant decrease in the consumption of this group.
- Among other antibacterials (ATC group J01X), consumption of glycopeptide antibacterials (J01XA) increased significantly in two countries (Denmark and Slovenia). A significant decrease was reported for Sweden.

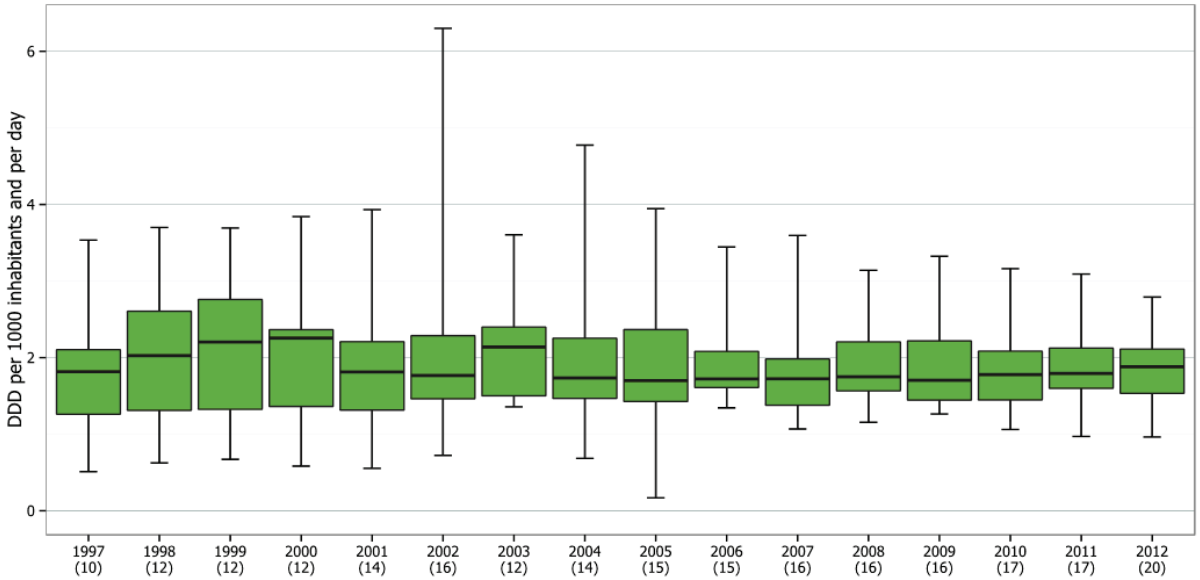
In 2012, the median consumption of antibacterials for systemic use (ATC group J01) was 1.9 DDD per 1 000 inhabitants and per day and was slightly higher than in recent years (Figure 4.2).

Table 4.2. Trends of consumption of antibacterials for systemic use (ATC group J01) in the hospital sector in EU/EEA countries, 2008–2012, expressed as DDD per 1 000 inhabitants and per day

Country	2008	2009	2010	2011	2012	Trends in antimicrobial consumption, 2008–2012	Average annual change 2008–2012	Statistical significance
Netherlands			1.1	1.0	1.0			n.a.
Bulgaria	1.5	1.6	1.4	1.4	1.4		-0.04	significant
Norway	1.7	1.5	1.4	1.5	1.4		-0.05	n.s.
Malta	1.4	1.4	2.0	1.7	1.4		0.03	n.s.
Portugal (b)		1.4	1.4	1.5	1.5			n.a.
Slovenia	1.7	1.8	1.7	1.7	1.6		-0.04	n.s.
Sweden	1.5	1.5	1.5	1.6	1.6		0.03	n.s.
Belgium	1.7		2.0	2.0	1.7			n.a.
Ireland	1.6	1.4	1.8	1.8	1.8		0.08	n.s.
Denmark	1.8	1.8	1.8	1.7	1.8		<0.01	n.s.
Croatia					2.0			n.a.
Luxembourg	2.3		2.1	2.0	2.0			n.a.
EU/EEA	**2.1**	**2.1**	**1.9**	**2.0**	**2.0**		**-0.01**	**n. s.**
Slovakia	1.8	1.9			2.0			n.a.
Greece		3.3		2.1	2.0			n.a.
Estonia	2.0	1.6	1.8	1.8	2.1		0.04	n.s.
France	2.2	2.2	2.2	2.1	2.1		-0.02	n.s.
Latvia	2.9	2.3	3.2	2.4	2.3		-0.12	n.s.
Lithuania					2.4			n.a.
Italy	2.3		2.1	2.3	2.4			n.a.
Finland (a)	3.1	3.2	2.8	3.1	2.8		-0.08	n.s.
Hungary	1.2	1.3	1.4					n.a.
Romania		2.6						n.a.

(a) Finland: data include consumption in remote primary healthcare centres and nursing homes.
(b) Portugal: data correspond to public hospitals only.
EU/EEA refers to the corresponding population-weighted mean consumption.
n.a.: not applicable: linear regression was not applied because data were not reported for all years 2008–2012.
n.s.: not significant.

Figure 4.2. Trends and inter-country variations of consumption of antibacterials for systemic use (ATC group J01) in the hospital sector, EU/EEA countries, 1997–2012, expressed as DDD per 1 000 inhabitants and per day



Boxes indicate the lower and the upper quartiles. The bold lines indicate the medians. Whiskers indicate the minimum and maximum values. For 1997–2009, only data from ESAC participating countries that also participated in ESAC-Net in 2012 are included. The number of participating countries is shown in parentheses.

Discussion

In 2012, the pattern of consumption of antibacterials for systemic use (ATC group J01) in the hospital sector was the same as in 2011. In contrast to consumption in the community (primary care), consumption in the hospital sector does not show a clear geographical gradient and the mean consumption has remained at about the same level since 2001. In line with this observation is the finding that only one of the countries showed a significantly decreasing or increasing trend over the five-year period 2008–2012.

The distribution of the consumption of antibacterials for systemic use (ATC group J01) between subgroups at the third ATC group level did not change from 2011 to 2012. Consumption of penicillins (ATC group J01C) and of other beta-lactam antibacterials (ATC group J01D, includes cephalosporins) accounted for nearly two thirds of the total consumption of antibacterials for systemic use (ATC group J01).

However, a substantial number of countries showed a significant increase in the consumption of last-line antibacterials such as carbapenems (ATC group J01DH) or glycopeptides (ATC group J01XA) during the five-year period 2008–2012. This included a significant increase in the EU/EEA population-weighted mean consumption for carbapenems.

In Finland, data from the hospital sector include consumption in remote primary healthcare centres and nursing homes, which results in a higher consumption rate than most other countries (Tables 4.1, 4.2 and A.2, and Figure 4.1).

4.2. Consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01BA)

Results

In 2012, 18 countries reported data on consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01BA) in the hospital sector (Table 4.3). The Netherlands reported on the consumption of antibacterials for systemic use (ATC group J01), but not on antimycotics or antifungals.

The EU/EEA population-weighted mean consumption was 0.14 DDD per 1 000 inhabitants and per day. Consumption varied by a factor of seven from 0.03 DDD per 1 000 inhabitants and per day (Lithuania) to 0.2 DDD per 1 000 inhabitants and per day (Denmark).

In 2012, amphotericin B (J02AA01) and fluconazole (J02AC01) accounted for 71% 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 22% (France) to 74% (Latvia). It made up more than 50% of the total consumption in 11 (61%) reporting countries.

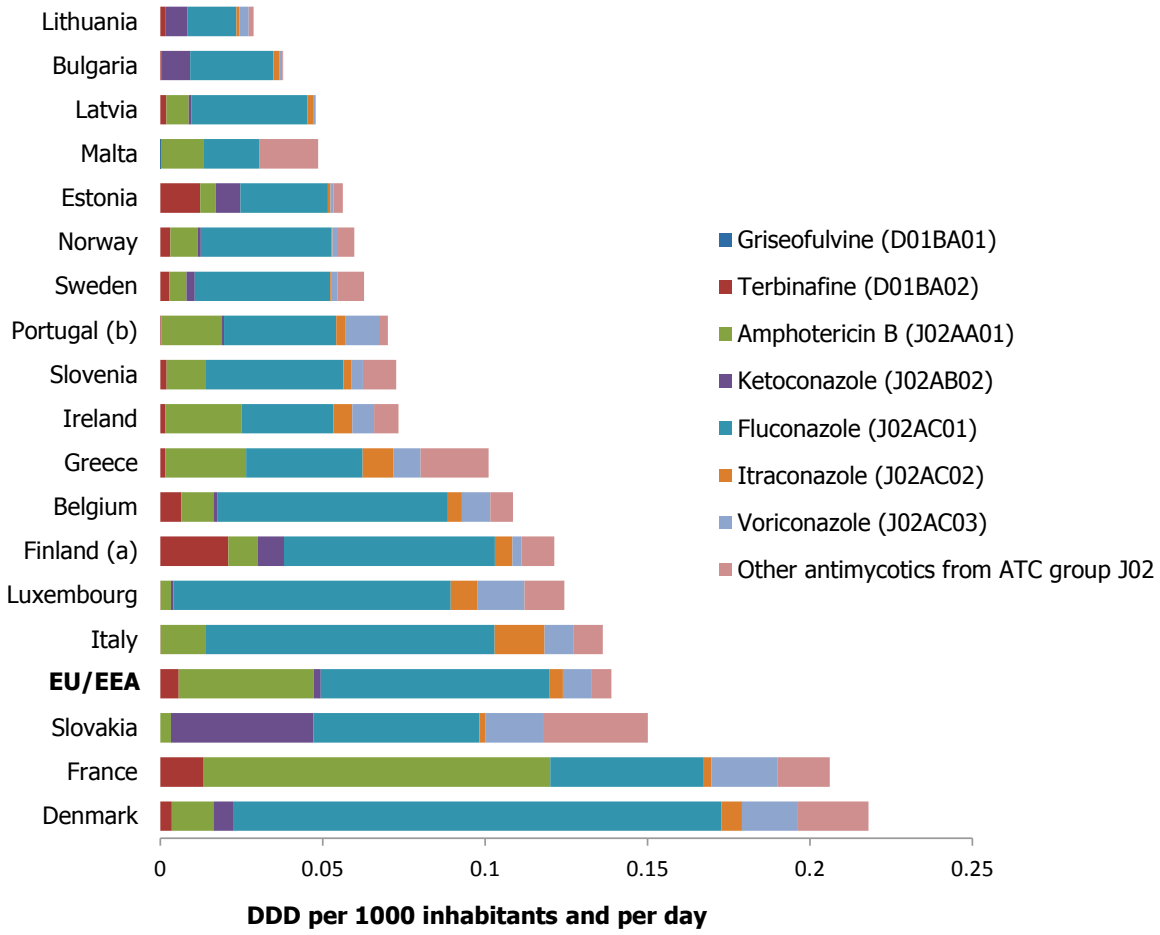
For Malta, no consumption was reported for ATC group D01BA as terbinafine is not on the Government Hospital Formulary List.

Table 4.3. Consumption of antimycotics (ATC group J02) and antifungals (ATC group D01BA) for systemic use in the hospital sector, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day

Country	Griseofulvine (D01BA01)	Terbinafine (D01BA02)	Amphotericin B (J02AA01)	Ketoconazole (J02AB02)	Fluconazole (J02AC01)	Itraconazole (J02AC02)	Voriconazole (J02AC03)	Other antimycotics for systemic use	Total (J02 & D01BA)
Belgium	0	0.007	0.010	0.001	0.071	0.004	0.009	0.007	0.109
Bulgaria	0	0.001	0	0.009	0.026	0.002	0.001	<0.001	0.038
Denmark	0	0.004	0.013	0.006	0.150	0.006	0.017	0.022	0.218
Estonia	0	0.012	0.005	0.008	0.027	0.001	0.001	0.003	0.056
Finland (a)	0	0.021	0.009	0.008	0.065	0.005	0.003	0.010	0.121
France	0	0.013	0.107	0	0.047	0.002	0.020	0.016	0.206
Greece	0	0.002	0.025	<0.001	0.036	0.010	0.008	0.021	0.101
Ireland	0	0.002	0.023	<0.001	0.028	0.006	0.007	0.008	0.073
Italy	0	<0.001	0.014	0	0.089	0.015	0.009	0.009	0.136
Latvia	0	0.002	0.007	0.001	0.036	0.002	0.001	<0.001	0.048
Lithuania	0	0.002	0	0.007	0.015	0.001	0.003	0.002	0.029
Luxembourg	0	<0.001	0.003	0.001	0.085	0.008	0.014	0.012	0.124
Malta	<0.001	0	0.013	<0.001	0.017	0	<0.001	0.018	0.049
Norway	0	0.003	0.009	0.001	0.040	<0.001	0.002	0.005	0.060
Portugal (b)	0	<0.001	0.019	0.001	0.035	0.003	0.010	0.003	0.070
Slovakia	0	0	0.003	0.044	0.051	0.002	0.018	0.032	0.150
Slovenia	0	0.002	0.012	<0.001	0.042	0.002	0.004	0.010	0.073
Sweden	0	0.003	0.005	0.003	0.042	<0.001	0.002	0.008	0.063
EU/EEA mean (population-weighted)	**<0.001**	**0.006**	**0.042**	**0.002**	**0.070**	**0.004**	**0.009**	**0.006**	**0.139**

(a) Finland: data include consumption in remote primary healthcare centres and nursing homes.
(b) Portugal: data correspond to public hospitals only.
EU/EEA refers to the corresponding population-weighted mean consumption based on the 18 countries that provided data.

Figure 4.3. Consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01BA) in the hospital sector, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day



(a) Finland: data include consumption in remote primary health care centres and nursing homes.
(b) Portugal: data correspond to public hospitals only.
EU/EEA refers to the corresponding population-weighted mean consumption based on the 18 countries that provided data.

Trends

The analysis of trends in the hospital consumption of antimycotics and antifungals for systemic use (ATC groups J02 & D01BA) during 2008–2012 included 18 countries and showed a significant increase in consumption for Denmark and Norway. The EU/EEA population-weighted mean consumption did not change significantly during the period.

Discussion

The pattern of consumption of antimycotics and antifungals for systemic use in the hospital sector was different from the community pattern. In the hospital sector, the prevailing substance was fluconazole as opposed to terbinafine in the community. The number of substances consumed in the hospital sector was also higher than in the community probably due to a broader diversity of infections and pathogens and a different case mix of the patients. However, the ratio of antimycotics and antifungals for systemic use over antibacterials for systemic use were similar both for the hospital sector and the community at around 6%.

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

Results

Twenty-four countries reported data to ESAC-Net on antivirals for systemic use (ATC group J05). The data are presented together for the community and the hospital sector (Table 5.1, 5.2 and Figure 5.1). Austria, the Czech Republic, Germany, Hungary and the Netherlands 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) was 2.1 DDD per 1 000 inhabitants and per day. Consumption showed an almost 33-fold difference from 0.14 DDD per 1 000 inhabitants and per day (Malta) to 4.65 DDD per 1 000 inhabitants and per day (Portugal).

The EU/EEA population-weighted mean consumption in the reporting countries was the highest for antivirals for treatment of HIV infections, combinations (ATC group J05AR) (0.74 DDD per 1 000 inhabitants and per day). Nucleosides and nucleotides excluding reverse transcriptase inhibitors (ATC group J05AB) and nucleoside and nucleotide reverse transcriptase inhibitors (ATC group J05AF) were the next most used groups both accounting for 0.39 DDD per 1 000 inhabitants and per day. For these three ATC groups (J05AR, J05AB, J05AF), France reported the highest consumption of all reporting countries with 1.4, 0.7 and 0.5 DDD per 1 000 inhabitants and per day, respectively. The lowest consumption of nucleosides and nucleotides excluding reverse transcriptase inhibitors (ATC group J05AB) was reported by Bulgaria (0.09 DDD per 1 000 inhabitants and per day). The lowest consumption of protease inhibitors (ATC group J05AE) was reported by Lithuania (<0.01 DDD per 1 000 inhabitants and per day). The lowest consumption of nucleoside and nucleotide reverse transcriptase inhibitors (ATC group J05AF) was reported by Malta (<0.01 DDD per 1 000 inhabitants and per day).

Table 5.2 and Figure 5.1 show the distribution of total consumption of antivirals for systemic use (ATC group J05) into seven categories based on their main indication: 'HIV/AIDS antivirals' 'HIV/hepatitis B antivirals', 'hepatitis C antivirals', 'herpes antivirals', 'influenza antivirals', and one group for remaining substances (see Annex 1).

The relative consumption of HIV/AIDS antivirals out of the total antiviral consumption ranged from 1.5% (Malta) to 84.3% (Estonia). The EU/EEA population-weighted mean consumption of HIV/AIDS antivirals accounted for 66% of the total consumption of antivirals for systemic use (ATC group J05) in the reporting countries.

Cyprus reported the highest proportion of consumption of HIV/hepatitis B antivirals (30%) and Greece of hepatitis B antivirals (24%). The proportion of the consumption of hepatitis C antivirals out of the total consumption of antivirals for systemic use (ATC group J05) ranged from 1.1% (the Netherlands) to 25.3% (Lithuania). For herpes antivirals, the proportion of total consumption of antivirals for systemic use (ATC group J05) ranged from 4.6% (Romania) to 86.2% (Malta).

In 2012, the highest consumption of oseltamivir (ATC code J05AH02) was 0.04 DDD per 1 000 inhabitants and per day in Finland, where it accounted for 1.5% of the total consumption of antivirals for systemic use (ATC J05) in that country. The EU/EEA population-weighted mean consumption for oseltamivir was 0.009 DDD per 1 000 inhabitants and per day.

Table 5.1. Total consumption of antivirals for systemic use (ATC group J05) in both sectors (community and hospital care sector), EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day

Country	Nucleosides and nucleotides excl. reverse transcriptase inhibitors (ATC group J05AB)	Protease inhibitors (ATC group J05AE)	Nucleoside and nucleotide reverse transcriptase inhibitors (ATC group J05AF)	Non-nucleoside reverse transcriptase inhibitors (ATC group J05AG)	Neura-minidase inhibitors (ATC group J05AH)	Antivirals for treatment of HIV infections, combinations (ATC group J05AR)	Other antivirals (ATC groups J05AC, J05AD, J05AX)	Total (ATC group J05)
Austria (a)	0.41	0.17	0.20	0.11	0.02	0.24	0.07	1.22
Belgium	0.14	0.37	0.21	0.23	0.01	0.80	0.08	1.84
Bulgaria	0.09	0.03	0.14	0.02	0.02	0.10	0.43	0.83
Cyprus	0.20	0.04	0.37	0.09	<0.01	0.21	0.02	0.93
Czech Republic (a)	0.21	0.01	0.15	0.02	<0.01	0.08	0.10	0.58
Denmark	0.50	0.29	0.27	0.23	<0.01	0.31	0.05	1.66
Estonia	0.31	0.37	0.20	0.58	0.01	1.14	0.03	2.64
Finland	0.41	0.12	0.06	0.07	0.04	0.45	0.04	1.19
France	0.71	0.67	0.48	0.32	0.02	1.40	0.28	3.88
Germany (a)	0.27	0.19	0.27	0.15	<0.01	0.57	0.09	1.56
Greece	0.28	0.16	0.96	0.06	0.01	0.43	0.06	1.97
Hungary (a)	0.17	0.02	0.10	0.03	<0.01	0.05	0.17	0.55
Iceland	0.51	0.12	0.04	0.04	0.02	0.39	0.01	1.13
Italy	0.44	0.51	0.62	0.22	<0.01	0.84	0.14	2.77
Latvia	0.26	0.10	0.11	0.19	0.01	0.25	0.21	1.12
Lithuania	0.14	<0.01	0.04	0.01	<0.01	0.03	0	0.23
Luxembourg	0.41	0.26	0.28	0.16	<0.01	0.89	0.14	2.14
Malta	0.14	0	<0.01	<0.01	<0.01	<0.01	0	0.14
Netherlands (a)	0.26	0.26	0.29	0.31	0	0.88	0.07	2.07
Norway	0.27	0.24	0.09	0.07	0.01	0.54	0.05	1.27
Portugal	0.35	1.21	0.87	0.81	<0.01	1.19	0.23	4.65
Romania	0.39	0.32	0.37	0.11	<0.01	0.45	0.18	1.81
Slovenia	0.23	0.05	0.13	0.06	0.01	0.08	0.02	0.58
Sweden	0.45	0.21	0.13	0.13	0.01	0.55	0.05	1.52
EU/EEA mean (population-weighted)	**0.39**	**0.37**	**0.39**	**0.21**	**0.01**	**0.74**	**0.15**	**2.25**

(a) Austria, the Czech Republic, Germany, Hungary and the Netherlands only reported consumption data from the community. EU/EEA refers to the corresponding population-weighted mean consumption based on the 24 countries that provided data.

Table 5.2. Total consumption of antivirals for systemic use (ATC group J05) from both sectors (community and hospital care sector), EU/EEA countries, grouped into categories of their main indication (adapted from [3] (see Annex 1), 2012, expressed as DDD per 1 000 inhabitants and per day

Country	HIV/AIDS antivirals	HIV/hepatitis B antivirals	Hepatitis B antivirals	Hepatitis C antivirals	Herpes antivirals	Influenza antivirals	Other antivirals	Total (ATC group J05)
Austria (a)	0.59	0.16	0.03	0.07	0.34	0.02	0	1.22
Belgium	1.51	0.13	0.05	0.04	0.10	0.01	<0.01	1.84
Bulgaria	0.15	0.08	0.06	0.04	0.05	0.02	0.43	0.83
Cyprus	0.40	0.28	0.05	0.05	0.16	<0.01	0	0.93
Czech Republic (a)	0.13	0.11	0.04	0.05	0.16	<0.01	0.09	0.58
Denmark	0.91	0.20	0.04	0.03	0.48	<0.01	0	1.66
Estonia	2.23	0.09	<0.01	0.18	0.14	0.01	0	2.64
Finland	0.69	0.04	<0.01	0.03	0.38	0.04	0	1.19
France	2.75	0.26	0.13	0.11	0.59	0.02	0	3.88
Germany (a)	1.03	0.15	0.10	0.08	0.20	<0.01	0	1.56
Greece	0.74	0.47	0.46	0.09	0.19	0.01	0.01	1.97
Hungary (a)	0.11	0.06	0.04	0.07	0.10	<0.01	0.16	0.55
Iceland	0.56	0.03	0.01	0.07	0.44	0.02	0	1.13
Italy	1.74	0.33	0.24	0.11	0.32	<0.01	0.01	2.77
Latvia	0.60	0.05	<0.01	0.19	0.06	0.21	0	1.12
Lithuania	0.04	0.02	0.02	0.06	0.08	<0.01	0	0.23
Luxembourg	1.48	0.13	0.11	0.10	0.31	<0.01	0.02	2.14
Malta	<0.01	<0.01	<0.01	0.01	0.12	<0.01	0	0.14
Netherlands (a)	1.55	0.17	0.09	0.02	0.23	0	0	2.07
Norway	0.91	0.05	0.03	0.07	0.20	0.01	<0.01	1.27
Portugal	3.66	0.48	0.15	0.10	0.24	<0.01	0	4.65
Romania	0.96	0.14	0.18	0.30	0.08	<0.01	0.14	1.81
Slovenia	0.21	0.03	0.10	0.04	0.19	0.01	0	0.58
Sweden	0.95	0.08	0.04	0.06	0.39	0.01	0	1.52
EU/EEA mean (population-weighted)	**1.48**	**0.21**	**0.13**	**0.10**	**0.29**	**0.01**	**0.03**	**2.25**

(a) Austria, the Czech Republic, Germany, Hungary and the Netherlands only reported consumption data from the community. EU/EEA refers to the corresponding population-weighted mean consumption based on the 24 countries that provided data.

Discussion

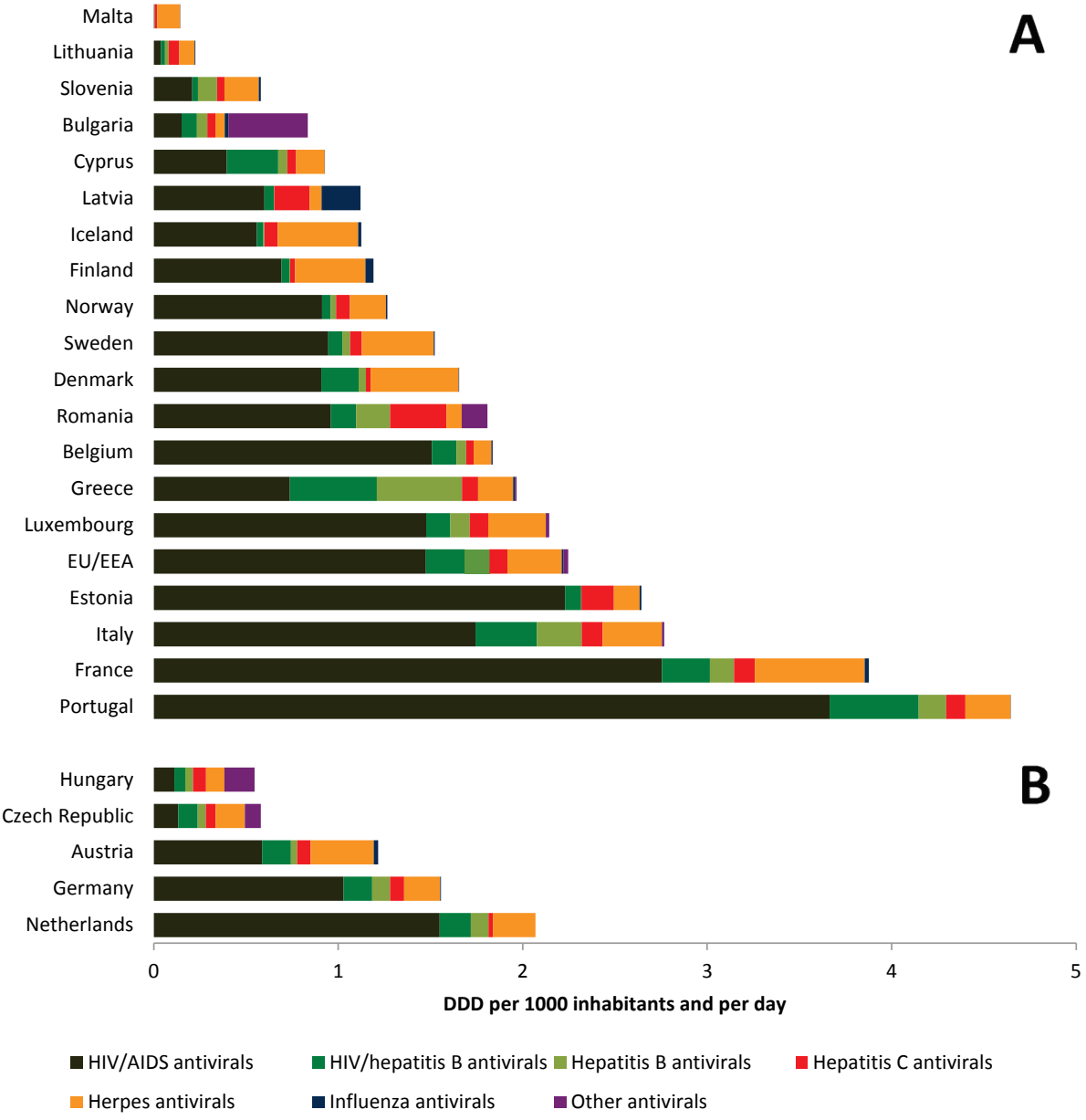
In contrast to the consumption of antibacterials for systemic use (ATC group J01) and of antimycotics and antifungals for systemic use (ATC groups J02 & D01BA), for which results are presented separately for each of the two healthcare sectors, consumption of antivirals for systemic use (ATC group J05) is presented for both sectors grouped together. A comparison of the European consumption of antivirals within one single sector would be less useful as the patterns of the distribution of total consumption of antivirals differ considerably between countries [16]. In some countries, the dispensing of certain antiviral classes is limited to the hospital sector. The reported total consumption of antivirals for systemic use (ATC group J05) in Austria, the Czech Republic, Germany, Hungary and the Netherlands is an underestimate since these countries did not report data on consumption in the hospital sector.

Within the ATC groups of antimicrobials for systemic use (ATC groups J01, J02 & D01BA, and J05), antivirals for systemic use (ATC group J05) showed the highest variation between countries. As shown for antibacterials for systemic use (ATC group J01), future data analysis may highlight certain socioeconomic or structural determinants that would explain these variations [17].

Following a suggestion from the ESAC project [3] to allocate the actual substances from the ATC classification into seven groups according to their main indication, this proposed classification was adopted by ESAC-Net to allow a more clinically relevant description of the consumption of antivirals for systemic use (Annex 1). The group 'HIV/AIDS antivirals' accounted for more than half of the total European consumption of antivirals for systemic use (ATC J05) and therefore consumption of this group is a major determinant of inter-country variations. Because antivirals are often used for the treatment of long-lasting infections similar to chronic diseases, data on consumption of antivirals may be interpreted differently from data on consumption of antibacterials. The large inter-country variation of total consumption of antivirals for systemic use (ATC group J05) may reflect the burden of viral infections rather than overuse or misuse as might be the case for antibacterials. For example, using data from 2008, the ESAC project showed a significant correlation between consumption of HIV/AIDS antivirals and the number of HIV/AIDS patients [3]. However, further analysis is needed to better understand variations of

consumption of HIV/AIDS antivirals across Member States. High consumption of antivirals could also be caused by the successful implementation of national strategies to improve the identification and treatment of patients with viral infections such as HIV.

Figure 5.1. Total consumption of antivirals for systemic use (ATC group J05), EU/EEA countries, grouped into categories of their main indication, 2012, expressed as DDD per 1 000 inhabitants and per day



EU/EEA refers to the corresponding population-weighted mean consumption based on the 24 countries that provided data. Total consumption of antivirals for systemic use from both sectors (A) (community and hospital care sector) and from the community only (B), (adapted from [3] (see Annex 1).

6 General discussion and perspectives

European countries increasingly implemented actions to control antimicrobial resistance in the community through rational use of antimicrobials, including awareness campaigns on the prudent use of antibiotics. Data provided by ESAC-Net reports for EU/EEA countries are deemed to be instrumental at national level for the evaluation of such campaigns, as were the ESAC project data in the past [10, 18].

The scope of ESAC-Net is to encourage all participants to report national antimicrobial consumption data at the medicinal product level by providing national registry data and the number of packages for each product. This standard version is the preferred format for reporting data to ESAC-Net as it allows for internal data validation and additional material for further analyses. For instance, the national registries include information on the number of individual products available on the market, which has been shown to be associated with the level of consumption [19]. In 2012, as in the two previous reports, two thirds of the reporting countries used this preferred format for reporting data. In addition, two countries (Denmark and Slovenia) provided data on community consumption stratified by age groups suggested by TESSy and on packages [16]. If more EU/EEA countries reported data stratified by age and on the number of packages consumed, it would be possible to identify the high consumers of certain antimicrobials in sub-groups of the population. Such differences and trends could provide targets for more specific interventions aimed at a more prudent use of antimicrobials in particular age groups. Quality of antimicrobial consumption data also 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 they do not include antimicrobials dispensed without a prescription and non-reimbursed prescribed antimicrobials [11]. For this reason, countries that report reimbursement data and that are known to have a substantial proportion of antimicrobials dispensed without a prescription, are indicated as such in the tables and figures in 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 in the consumption rates reported. However, the number of countries that each year change data provider and/or types of data is small. In 2012, 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 because sales data include consumption without prescription or other non-reimbursed courses.

A standardised reporting protocol is essential to ensure comparability with other multinational surveillance networks. The ESAC-Net reporting protocol was built upon the former ESAC project. Very recently a cross-national database study with the WHO Regional Office for Europe was published providing antimicrobial consumption (combined community and hospital sector) from 13 non-EU, southern and eastern European countries. This new surveillance system applied the same reporting protocol as ESAC-Net and thus enabled comparability of data with that from EU/EEA countries [20].

In 2012, 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 [21]. A gradual increase in the median overall consumption in the community was reported by the ESAC project between 2004 and 2008. However, this report shows that the EU/EEA population-weighted mean consumption in the community did not increase significantly during the period 2008–2012.

The overall consumption of antibacterials for systemic use (ATC group J01) did not change significantly during this period in most of the countries; only five countries showed a significant increase and one country showed a significant decrease. However, the trend analyses of subgroups of antibacterials for systemic use revealed significant trends in the consumption of penicillins in more than half of the countries included in the analyses, e.g. indicating 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).

A second antimicrobial consumption indicator, i.e. 'packages per 1 000 inhabitants and per day', was used for community consumption of orally administered antibacterials for systemic use (ATC group J01) in 20 countries. The changes in the ranking positions of some countries compared with their ranking when reporting 'DDD per 1 000 per inhabitants and per day' indicate the need for more than one single indicator to correctly describe antimicrobial consumption in EU/EEA countries. Very recently, a study suggested that for countries dispensing complete packages for community prescriptions such as Belgium, consumption data expressed in 'packages per 1 000 inhabitants and per day' might be a more appropriate measurement unit to use when assessing trends in prescribing of antibacterial agents and the impact of antibiotic awareness campaigns [4].

The former ESAC project developed and published 12 quality indicators for antimicrobial consumption in the community, based on a consensus of European antimicrobial surveillance experts [2]. Data on these consensus-based quality indicators are reported by ESAC-Net but, as stated in the report summary, comparisons between countries should be made with caution. Nevertheless, these indicators could be used by healthcare professionals and policy makers to monitor progress towards a more prudent use of antibiotics in the community.

For the hospital sector, the types of healthcare settings that are included differ across European 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 2012, include consumption from nursing homes and from remote primary healthcare centres. For this reason, antimicrobial consumption from the hospital sector in Finland cannot be compared with that of other countries. It should be emphasised that the number of countries reporting data specifically for the hospital sector is increasing. In 2012, two additional countries reported data from the hospital sector for the first time to ESAC-Net (see Chapter 2.3, Annex 2, Table A2).

Reliable national data on antimicrobial consumption are paramount for our understanding of the epidemiology of antimicrobial resistance because they provide information on the ecological selection pressure due to antimicrobial use. Settings, i.e. countries, regions or hospitals, reporting a high consumption generally also have a higher level of antimicrobial resistance than settings reporting a low consumption. Healthcare-associated infections with *Klebsiella pneumoniae* that have become resistant to multiple agents, including to last-line antimicrobials such as carbapenems, are now prevalent in hospitals in some EU/EEA countries. At the level of each individual hospital, specific antimicrobial resistance problems are reported depending on the patient case-mix, varying infection prevention and control practices, and antimicrobial prescribing practices. There is a need to improve surveillance of antimicrobial consumption at the level of each individual hospital in EU/EEA countries.

For the time being, ESAC-Net uses the same measurement unit (i.e., DDD per 1 000 inhabitants and per day) for reporting antimicrobial consumption in the community and in the hospital sector. Development of a specific module for hospital-level surveillance of antimicrobial consumption presents the next challenge for ESAC-Net. ESAC-Net set up a working group to develop a protocol to collect consumption data at the hospital level by using additional denominators for hospital consumption. Such developments should enable the identification of areas for improvement, which could be addressed by national, regional and local antimicrobial stewardship programmes. The introduction of a unique hospital identifier for data reporting would allow hospital antimicrobial consumption data from ESAC-Net to be linked with antimicrobial resistance data from the European Antimicrobial Resistance Surveillance Network (EARS-Net) as well as data on healthcare-associated infections from the Healthcare-associated Infections surveillance Network (HAI-Net).

Unlike the consumption of antibacterials for systemic use (ATC group J01) and of antimycotics and antifungals for systemic use (ATC groups J02 & D01BA), for which results are presented separately for the community and for the hospital sector, consumption of antivirals for systemic use (ATC group J05) was reported for both sectors grouped together. While the distribution of consumption of antimicrobials of the ATC groups J01 and J02 & D01BA shows that the largest proportion of consumption takes place in the community, the largest consumption of antivirals may take place in the community or in the hospital sector, depending on the country. In several countries, the dispensing of certain groups of antivirals is limited to the hospital sector, although the patients may be treated in the community. To some extent, surveillance of antiviral consumption shows an essential difference compared to the consumption of antibacterials, as antivirals are often used for the treatment of long-lasting infections similar to chronic diseases. In 2012, consumption of antivirals showed the highest inter-country variation of all three main antimicrobial groups under surveillance, and may reflect the burden of viral diseases rather than targets for improving practices and a more prudent use of antiviral agents.

At this stage, data collected by the ESAC project and by ECDC on drugs for the treatment of tuberculosis (ATC group J04A), use of oral and rectal nitroimidazole derivates as antiprotozoals (ATC group P01AB), and oral vancomycin used as a non-absorbable intra-intestinal antiinfective (ATC A07AA09) are only available to ESAC-Net participants via the TESSy database access. The data on drugs from ATC group J04, particularly, will require validity and quality checks before they are made publicly available in a separate chapter of this report.

This ESAC-Net report only presents antimicrobial consumption by humans. Data on the sales of veterinary antimicrobial agents used in animals are produced by the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project [22]. Consumption of antimicrobials both in humans and in animals is associated with the development and spread of antimicrobial resistance. Inter-agency work currently aims to integrate data on antimicrobial consumption and on antimicrobial resistance in humans and in animals into a single European report.

References

1. 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.

2. 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.

3. Adriaenssens N, Coenen S, Kroes AC, Versporten A, Vankerckhoven V, Muller A, et al. European Surveillance of Antimicrobial Consumption (ESAC): systemic antiviral use in Europe. J Antimicrob Chemother. 2011 Aug;66(8):1897-905.

4. Coenen S, Gielen B, Blommaert A, Beutels P, Hens N, Goossens H. Appropriate international measures for outpatient antibiotic prescribing and consumption: recommendations from a national data comparison of different measures. J Antimicrob Chemother. 2013 Oct 1.

5. European Centre for Disease Prevention and Control [Internet]. Antimicrobial interactive database (ESAC-Net). Available from: http://ecdc.europa.eu/en/activities/surveillance/esac-net/pages/index.aspx.

6. European Centre for Disease Prevention and Control [Internet]. Healthcare-Associated Infections surveillance network (HAI-Net). Available from: http://ecdc.europa.eu/en/activities/surveillance/HAI/Pages/default.aspx.

7. Adriaenssens N, Coenen S, Versporten A, Muller A, Minalu G, Faes C, et al. European Surveillance of Antimicrobial Consumption (ESAC): outpatient quinolone use in Europe (1997-2009). J Antimicrob Chemother. 2011 Dec;66 Suppl 6:vi47-56.

8. Adriaenssens N, Coenen S, Versporten A, Muller A, Minalu G, Faes C, et al. European Surveillance of Antimicrobial Consumption (ESAC): outpatient macrolide, lincosamide and streptogramin (MLS) use in Europe (1997-2009). J Antimicrob Chemother. 2011 Dec;66 Suppl 6:vi37-45.

9. European Centre for Disease Prevention and Control. ESAC-Net reporting protocol (for 2013 data). Version 4. Stockholm: ECDC; 2014. Available from: http://www.ecdc.europa.eu/en/activities/surveillance/ESAC-Net/publications/Documents/antimicrobial-consumption-ESAC-Net-reporting-protocol-2014.pdf.

10. ESAC Management Team, the ESAC Scientific Advisory Board and the ESAC National Networks. ESAC Yearbook 2009. 2011. Available from http://ecdc.europa.eu/en/activities/surveillance/esac-net/publications/documents/esac_yearbook_2009.pdf

11. Safrany N, Monnet DL. Antibiotics obtained without a prescription in Europe. Lancet Infect Dis. 2012 Mar;12(3):182-3.

12. Coenen S, Adriaenssens N, Versporten A, Muller A, Minalu G, Faes C, et al. European Surveillance of Antimicrobial Consumption (ESAC): outpatient use of tetracyclines, sulphonamides and trimethoprim, and other antibacterials in Europe (1997-2009). J Antimicrob Chemother. 2011 Dec;66 Suppl 6:vi57-70.

13. Versporten A, Coenen S, Adriaenssens N, Muller A, Minalu G, Faes C, et al. European Surveillance of Antimicrobial Consumption (ESAC): outpatient penicillin use in Europe (1997-2009). J Antimicrob Chemother. 2011 Dec;66 Suppl 6:vi13-23.

14. Versporten A, Coenen S, Adriaenssens N, Muller A, Minalu G, Faes C, et al. European Surveillance of Antimicrobial Consumption (ESAC): outpatient cephalosporin use in Europe (1997-2009). J Antimicrob Chemother. 2011 Dec;66 Suppl 6:vi25-35.

15. Adriaenssens N, Coenen S, Muller A, Vankerckhoven V, Goossens H. European Surveillance of Antimicrobial Consumption (ESAC): outpatient systemic antimycotic and antifungal use in Europe. J Antimicrob Chemother. 2010 Apr;65(4):769-74.

16. European Centre for Disease Prevention and Control. Surveillance of antimicrobial consumption in Europe, 2010. Stockholm: ECDC; 2013. Available from: http://ecdc.europa.eu/en/publications/Publications/Forms/ECDC_DispForm.aspx?ID=1068E.

17. Blommaert A, Marais C, Hens N, Coenen S, Muller A, Goossens H, et al. Determinants of between-country differences in ambulatory antibiotic use and antibiotic resistance in Europe: a longitudinal observational study. J Antimicrob Chemother. 2013 Sep 29.

18. Adriaenssens N, Coenen S, Versporten A, Muller A, Minalu G, Faes C, et al. European Surveillance of Antimicrobial Consumption (ESAC): outpatient antibiotic use in Europe (1997-2009). J Antimicrob Chemother. 2011 Dec;66 Suppl 6:vi3-12.

19. Monnet DL, Ferech M, Frimodt-Moller N, Goossens H. The more antibacterial trade names, the more consumption of antibacterials: a European study. Clin Infect Dis. 2005 Jul 1;41(1):114-7.

20. 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 19.

21. Borg MA. Cultural determinants of infection control behaviour: understanding drivers and implementing effective change. J Hosp Infect. 2014 Jan 14.

22. European Medicines Agency. Sales of veterinary antimicrobial agents in 25 EU/EEA countries in 2011. Third ESVAC report. (EMA/236501/2013) London: EMA; 2013.

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

Classification of macrolides into short-, intermediate- and long-acting macrolides*

Short-acting		Intermediate-acting		Long-acting	
ATC code	**Substance**	**ATC code**	**Substance**	**ATC code**	**Substance**
J01FA01	erythromycin	J01FA06	roxithromycin	J01FA10	azithromycin
J01FA02	spiramycin	J01FA07	josamycin	J01FA13	dirithromycin
J01FA03	midecamycin	J01FA09	clarithromycin		
J01FA05	oleandomycin	J01FA14	flurithromycin		
J01FA08	troleandomycin	J01FA15	telithromycin		
J01FA11	miocamycin				
J01FA12	rokitamycin				

**Macrolides subdivided into short-acting (half-life <4h), intermediate-acting (half-life 4–24h) and long-acting (half-life >24h) macrolides. Adapted from [8].*

Classification of quinolones into three generations*

First generation		Second generation		Third generation	
J01MA06	norfloxacin	J01MA01	ofloxacin	J01MA05	temafloxacin
J01MB01	rosoxacin	J01MA02	ciprofloxacin	J01MA13	trovafloxacin
J01MB02	nalidixic acid	J01MA03	pefloxacin	J01MA14	moxifloxacin
J01MB03	piromidic acid	J01MA04	enoxacin	J01MA15	gemifloxacin
J01MB04	pipemidic acid	J01MA07	lomefloxacin	J01MA16	gatifloxacin
J01MB05	oxolinic acid	J01MA08	fleroxacin	J01MA17	prulifloxacin
J01MB06	cinoxacin	J01MA09	sparfloxacin	J01MA18	pazufloxacin
J01MB07	flumequine	J01MA10	rufloxacin	J01MA19	garenoxacin
		J01MA11	grepafloxacin	J01MA21	sitafloxacin
		J01MA12	levofloxacin		

** Classification of quinolones is based on their chemical structure and antimicrobial activity. Adapted from [7].*

Classification of antivirals into seven groups based on their main indication*

Substances used for the treatment of influenza: 'influenza antivirals'

J05AC02	rimantadine	J05AH01	zanamivir	J05AH02	oseltamivir

Substances used for the treatment of hepatitis C: 'hepatitis C antivirals'

J05AB04	ribavirin	J05AE11[(a)]	telaprevir	J05AE12	boceprevir

Substances used for the treatment of herpetic infections: 'herpes antivirals'

J05AB01	aciclovir	J05AB09	famciclovir	J05AB14	valganciclovir
J05AB02	idoxuridine	J05AB11	valaciclovir	J05AB15	brivudine
J05AB03	vidarabine	J05AB12	cidofovir	J05AC03	tromantadine
J05AB06	ganciclovir	J05AB13	penciclovir	J05AD01	foscarnet

Substances used for the treatment of HIV/AIDS: 'HIV/AIDS antivirals'

J05AE01	saquinavir	J05AF04	stavudine	J05AR05[(a)]	zidovudine, lamivudine and nevirapine
J05AE02	indinavir	J05AF06	abacavir	J05AR06	emtricitabine, tenofovir disoproxil and efavirenz
J05AE03	ritonavir	J05AG01	nevirapine	J05AR07[(a)]	stavudine, lamivudine and nevirapine
J05AE04	nelfinavir	J05AG01	nevirapine	J05AR08	emtricitabine, tenofovir disoproxil and rilpivirine
J05AE05	amprenavir	J05AG02	delavirdine	J05AR09	emtricitabine, tenofovir disoproxil, elvitegravir and cobicistat
J05AE07	fosamprenavir	J05AG03	efavirenz	J05AR10	lopinavir and ritonavir
J05AE08	atazanavir	J05AG04	etravirine	J05AX07	enfuvirtide
J05AE09	tipranavir	J01AG05[(a)]	rilpirivine	J05AX08[(a)]	raltegravir
J05AE10	darunavir	J05AR01	zidovudine and lamivudine	J05AX09[(a)]	maraviroc
J05AF01	zidovudine	J05AR02	lamivudine and abacavir	J05AX11[(a)]	elvitegravir
J05AF02	didanosine	J05AR03	tenofovir disoproxil and emtricitabine	J05AX12[(a)]	dolutegravir
J05AF03	zalcitabine	J05AR04	zidovudine, lamivudine and abacavir		

Substances used for the treatment of hepatitis B: 'hepatitis B antivirals'

J05AF08	adefovir dipivoxil	J05AF11	telbivudine
J05AF10	entecavir	J05AF12	clevudine

Substances used for both HIV and hepatitis B treatment: 'HIV/hepatitis B antivirals'

J05AF05	lamivudine	J05AF07	tenofovir disoproxil	J05AF09	emtricitabine

'Other antivirals'

J05AA01[(a)]	metisazone	J05AX02	lysozyme	J05AX10[(a)]	maribavir
J05AD02[(a)]	fosfonet	J05AX05	inosine pranobex		
J05AX01	moroxydine	J05AX06	Pleconaril		

* Adapted from [3];
(a) zero consumption reported from all ESAC-Net participants.

This classification is not part of that of the WHO Collaborating Centre for Drug Statistics Methodology.

Annex 2. Additional data

Table A1. Consumption of antibacterials for systemic use (ATC group J01) in the community, EU/EEA countries, 1997–2012, expressed as DDD per 1 000 inhabitants and per day

Country	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Austria		12.6	13.1	12.3	11.8	11.8	12.5	12.6	14.5	14.3	14.7	15.1	15.5	15.0	14.5	13.9
Belgium	25.4	26.4	26.2	25.3	23.7	23.8	23.8	22.8	24.3	24.2	25.4	27.8	27.5	28.4	29.0	29.8
Bulgaria			15.1*	20.2*	22.7*	17.3*	15.5*	16.4*	18.0*	17.7	19.4	20.3	18.3	18.2	19.5	18.5
Croatia																21.7
Cyprus										31.9*	33.9*	32.9*	34.4*	31.0*	32.0*	29.7*
Czech Republic		18.2	18.6				16.7	15.9	17.3	15.9	16.5	17.5	18.4	17.9	18.5	17.5
Denmark	12.2	12.7	12.1	12.3	12.8	13.2	13.5	14.1	14.6	15.2	15.9	15.6	15.6	16.5	17.4	16.4
Estonia					14.4*	11.7	11.1	10.4	11.7	11.4	12.2	11.9	11.1	11.1	12.1	11.6
Finland	19.4	18.4	18.4	19.1	19.8	17.9	18.7	17.3	18.1	17.4	18.3	17.8	17.9	18.5	20.1	19.5
France	33.1	33.6	34.1	33.3	33.2	32.2	28.9	27.1	28.9	27.9	28.6	28.1	29.6	28.2	28.7	29.7
Germany	13.0	13.3	13.6	13.7	12.8	12.7	13.9	13.0	14.6	13.6	14.5	14.6	14.9	14.5	14.1	14.9
Greece	25.1	24.9	28.5	29.5	29.6	30.6	31.3	33.1*	34.7*	41.0*	43.1*	45.3*	38.6	39.4*	35.1	31.9
Hungary		18.3	23.5	18.6	18.6	17.1	19.1	18.2	19.5	17.2	15.5	15.2	16.0	15.7	14.7	13.8
Iceland	22.2*	23.1*	21.7*	20.5*	20.0*	20.6*	20.3*	21.5*	23.2*	20.0	19.2	20.7	19.4	22.3*	22.3*	22.1*
Ireland		16.5	18.0	17.6	18.7	18.7	20.1	20.3	20.5	21.2	22.9	22.5	20.8	20.3	22.6	23.0
Italy			24.5	24.0	25.5	24.3	25.6	24.8	26.2	26.7	27.6	28.5	28.7	27.3	27.6	27.6
Latvia						11.2		12.0	12.5	11.5	12.4	11.4	10.9	11.8	12.8	13.1
Lithuania										22.7*	24.1*	25.1*	19.5*	17.7*	19.0*	16.2
Luxembourg (a)	27.2	26.9	28.2	27.2	27.6	27.5	28.6	25.0	26.3	25.1	27.2	27.1	28.2	28.6	27.6	27.9
Malta											17.9	20.9	21.6	21.3	23.4	22.5
Netherlands	10.1	9.9	10.0	9.8	9.9	9.8	9.8	9.8	10.5	10.8	11.0	11.2	11.4	11.2	11.4	11.3
Norway		15.3			15.6	15.7	15.6	15.7	16.8	14.8	15.5	15.6	15.2	15.8	16.5	16.9
Poland		20.7	22.2	22.7	24.8	21.4		19.1	19.6		22.2	20.7	23.6	21.0	21.9	19.8
Portugal	23.1	23.3	25.2	24.9	24.5	26.5	25.1	23.8	24.5	22.7		22.7	22.9	22.4	23.2	22.7
Romania (c)													10.2		30.9*	30.4*
Slovakia			25.7	27.7	29.1	26.7	27.6	22.6	25.1	22.5	24.8	23.2	23.8		23.8*	20.0
Slovenia	17.5	19.3	19.8	18.1	17.4	16.3	17.0	16.8	16.3	14.7	16.0	14.9	14.3	14.4	14.4	14.3
Spain (b)	21.3	20.6	20.0	19.0	18.0	18.0	18.9	18.6	19.3	18.7	19.9	19.8	19.7	20.3	20.9	20.9
Sweden	14.6	15.5	15.8	15.6	15.8	15.2	14.7	14.5	14.9	15.4	15.5	14.6	14.1	14.2	14.3	14.1
United Kingdom	17.0	16.2	14.8	14.3	14.8	14.8	15.1	15.0	15.4	15.3	16.5	17.0	17.3	18.6	18.8	20.0
EU/EEA mean (population-weighted)	**20.0**	**19.7**	**20.6**	**20.4**	**20.5**	**19.8**	**19.7**	**19.0**	**20.1**	**19.9**	**20.8**	**21.0**	**20.9**	**20.9**	**21.5**	**21.5**

**Total care data; i.e. including the hospital sector.*
(a) Luxembourg updated all years with insured population data.
(b) Spain provided reimbursement data, i.e. not including consumption without a prescription and other non-reimbursed courses.
(c) Romania re-uploaded separated community and hospital sector data for 2011 as total care data (see Table A2).

Table A2. Consumption of antibacterials for systemic use (ATC group J01) in the hospital care sector, EU/EEA countries, 1997–2012, expressed as DDD per 1 000 inhabitants and per day

Country	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Belgium	2.0	2.0	2.2	2.2	2.2	2.2	2.3	2.1	1.9	1.9	1.9	1.7		2.0	2.0	1.7
Bulgaria										1.4	1.4	1.5	1.6	1.4	1.4	1.4
Croatia																2.0
Denmark	1.3	1.3	1.3	1.4	1.4	14	1.5	1.6	1.6	1.7	1.8	1.8	1.8	1.8	1.7	1.8
Estonia						2.1	2.4	2.3	2.5	1.9	1.8	2.0	1.6	1.8	1.8	2.1
Finland (a)	3.5	3.7	3.7	3.8	3.9	3.9	3.6	3.4	3.5	3.4	3.2	3.1	3.2	2.8	3.1	2.8
France	3.3	3.0	3.0	3.2	2.9	3.9	2.8	2.5	2.6	2.3	2.2	2.2	2.2	2.2	2.1	2.1
Greece	2.1	2.1	21	2.3	2.2	2.2	2.3						3.3		2.1	2.0
Hungary					1.2	1.2	1.5	1.3	1.4	1.4	1.2	1.2	1.3	1.3		
Ireland								0.7	0.7	1.9	1.1	1.6	1.4	1.8	1.8	1.8
Italy									0.2		1.5	2.3		2.1	2.5	2.5
Latvia						6.3		4.8	3.9	3.2	3.6	2.9	2.3	3.2	2.4	2.3
Lithuania														2.4		2.4
Luxembourg	2.1	2.0	2.3	2.3	2.1	2.5	2.5	2.1	2.2	2.2	2.3	2.3		2.1	2.1	2.0
Malta	1.6	2.5	2.6	2.4	1.9	1.7	2.0	1.8	1.4	1.7	1.3	1.4	1.4	2.0	1.7	1.4
Netherlands	0.6	0.6	0.7	0.6	0.6	0.7								1.1	1.0	1.0
Norway		1.1			1.1	1.3	1.4	1.3	1.3	1.5	1.5	1.7	1.5	1.4	1.5	1.4
Poland		3.0	3.4	2.4	2.4	1.7										
Portugal (b)													1.4	1.4	1.4	1.5
Romania (c)													2.6			
Slovakia			1.3	1.2	1.4	1.5	1.4	1.6	1.9	1.7	1.9	1.8	1.9			2.0
Slovenia	0.5	1.6	1.7	1.8	1.7	1.8	1.8	1.6	1.7	1.7	1.7	1.7	1.8	1.7	1.7	1.6
Sweden	1.3	1.3	1.3	1.3	1.3	1.3	1.4	1.4	1.5	1.5	1.3	1.5	1.5	1.5	1.6	1.6
EU/EEA mean (population-weighted)	**2.4**	**2.5**	**2.6**	**2.4**	**2.2**	**2.5**	**2.4**	**2.2**	**1.6**	**2.1**	**1.8**	**2.1**	**2.1**	**1.9**	**2.0**	**2.0**

(a) Finland: data include consumption in remote primary healthcare centres and nursing homes.
(b) Portugal: data correspond to public hospitals only.
(c) Romania re-uploaded separated community and hospital sector data for 2011 as total care data (see Table A1).