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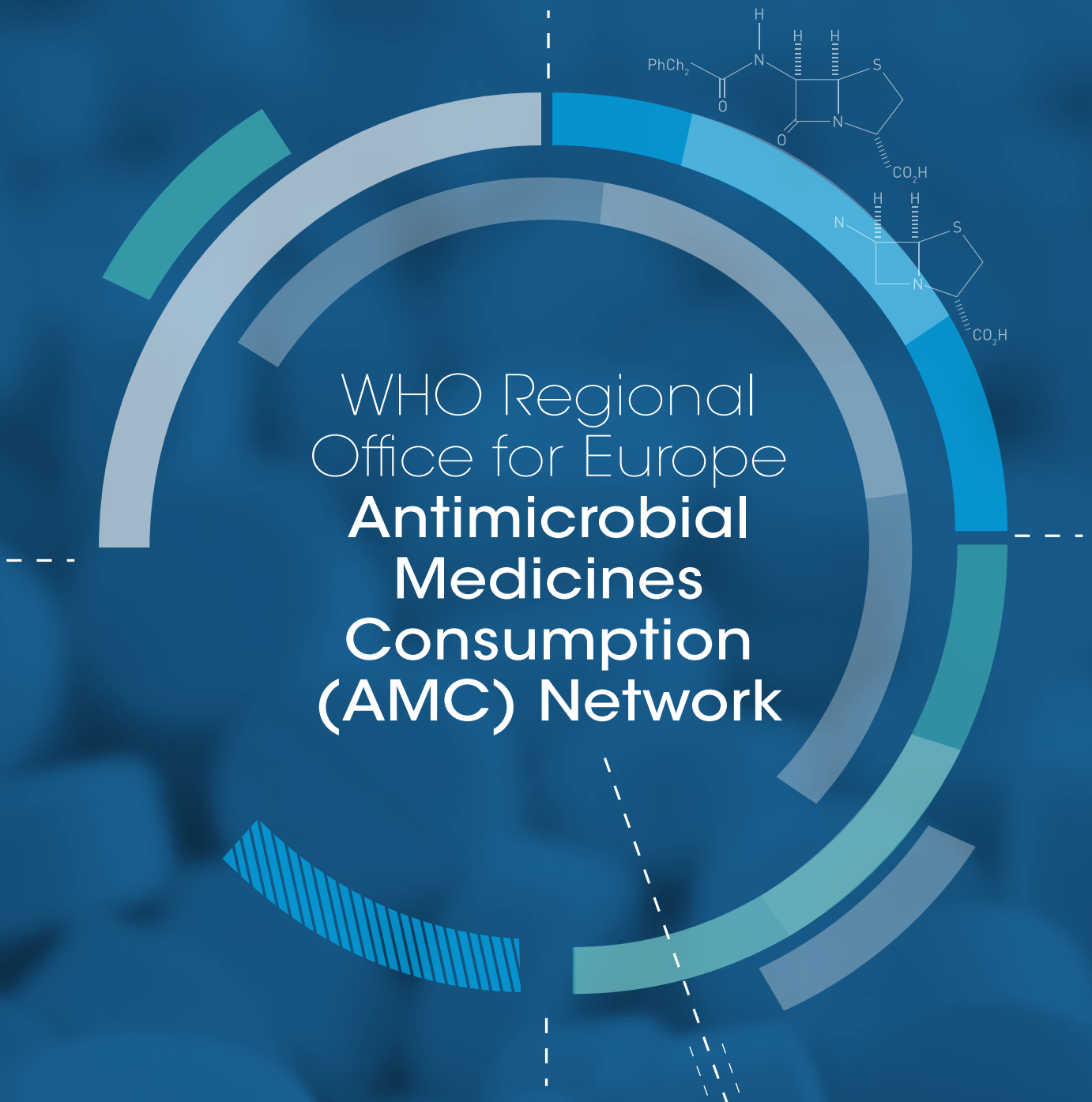

WHO Regional Office for Europe Antimicrobial Medicines Consumption (AMC) Network

AMC data 2011–2014

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Abstract

This report sets out and analyses data on antimicrobial medicines consumption (AMC) collected from non-European Union countries in the WHO European Region and Kosovo (in accordance with Security Council resolution 1244 (1999)). Its aims are to support countries that are building or strengthening their national surveillance systems on AMC and to stimulate the sharing of data both within and between countries. The WHO Regional Office for Europe and its partners remain committed to supporting countries in these endeavours through the activities of the WHO AMC Network.

Keywords

ANTIMICROBIAL MEDICINES CONSUMPTION
NATIONAL SURVEILLANCE NETWORKS
ANTI-INFECTIVE AGENTS – THERAPEUTIC USE
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CONTENTS

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FOREWORD

In September 2011, all 53 countries in the WHO European Region adopted the European strategic action plan on antibiotic resistance. Strategic priorities included strengthening of the surveillance of antibiotic resistance and antimicrobial consumption and promoting the rational use of antimicrobial medicines. The WHO Global Action Plan on antimicrobial resistance was agreed by Members States at the Sixty-eighth World Health Assembly in 2015. It recognizes the importance of collecting and analysing data on antibiotic use as a means of identifying potential overuse, underuse and inappropriate use of antimicrobial medicines, and as a basis for developing interventions to address inappropriate practices.

Such actions are key to the WHO Regional Office for Europe's agenda on strengthening health systems in order to accelerate health gains and reduce health inequalities. This health systems strengthening agenda was endorsed by all Member States via the 2008 Tallinn Charter (Health Systems for Health and Wealth) and is a priority area under Health 2020, the European policy for health and well-being. Improving health information and health information systems – collating, interpreting and analysing data, and using the results to inform decision-making – is central to this work.

Surveillance of AMC has been undertaken by all countries of the European Union (EU), as well as Iceland and Norway, via the European Surveillance on Antimicrobial Consumption Network (ESAC-Net) since 1997. This work is now coordinated by ECDC, but surveillance of antimicrobial consumption in the non-EU Member States in the WHO European Region has not been systematic.

To address this, the WHO Regional Office for Europe established the WHO AMC Network in 2011 to assist countries in setting up or strengthening national AMC surveillance and to contribute to Region-wide AMC surveillance. A national approach to monitoring and evaluation ultimately serves to provide centralized data to ensure that policies and strategies to address AMC and antimicrobial resistance are effective. These efforts are closely coordinated with ECDC to ensure that data are comparable and compatible, which will provide a pan-European overview of trends and sources of AMC.

This report describes the data collected from a number of non-EU countries in the WHO European Region gathered through the WHO AMC Network. Its aim is to illustrate the value of national AMC surveillance and to stimulate the sharing of data both within and between countries. Sharing of these data show that national governments are taking antimicrobial resistance seriously as a key public health issue.

The WHO Regional Office for Europe remains committed to supporting countries in these endeavours through the activities of the WHO AMC Network.

Hans Kluge, MD
Director, Division of Health Systems and Public Health

ABBREVIATIONS

AMC	antimicrobial medicines consumption
ATC	Anatomical Therapeutic Chemical (classification system)
CAESAR	Central Asian and Eastern European Surveillance of Antimicrobial Resistance (Network)
DDD	defined daily dose
DID	defined daily doses per 1000 inhabitants per day
ECDC	European Centre for Disease Prevention and Control
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
EU	European Union

Abbreviations of country and area names used in some tables and figures

ALB	Albania
ARM	Armenia
AZE	Azerbaijan
BLR	Belarus
KGZ	Kyrgyzstan
MDA	Republic of Moldova
MNE	Montenegro
SRB	Serbia
TJK	Tajikistan
TUR	Turkey
UZB	Uzbekistan
KOS	Kosovo (in accordance with Security Council resolution 1244 (1999))

SUMMARY

The WHO AMC Network is an initiative of the WHO Regional Office for Europe. It aims to support all countries in the WHO European Region that are not part of the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) coordinated by the European Centre for Disease Prevention and Control (ECDC).

Albania, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Georgia, Kazakhstan, Kyrgyzstan, Montenegro, the Republic of Moldova, the Russian Federation, Serbia, Tajikistan, the former Yugoslav Republic of Macedonia, Turkey, Ukraine and Uzbekistan, as well as Kosovo,[1] are currently engaged at various stages of participation in the WHO AMC Network. Between 2011 and 2014, all of these contributed one or more years of antimicrobial consumption data to the Network.

This is the first WHO AMC Network report; it sets out and analyses the antimicrobial consumption data for 11 of the participating countries and Kosovo.[1]

Key findings

Data on total consumption of antibacterials for systemic use (Anatomical Therapeutic Chemical (ATC) classification group J01) was available for 11 countries and Kosovo.[1] Consumption in 2014 ranged from 8.5 defined daily doses per 1000 inhabitants per day (DID) in Azerbaijan to 40.4 DID in Turkey– a more than fourfold difference in consumption estimates. The population-weighted mean consumption across the 12 datasets was 24.4 DID.

Even greater variability was reported in the relative use of parenteral (injectable) formulations – from 4% of total J01 consumption in Turkey to 69% in Azerbaijan.

The most commonly consumed subgroup of antibacterials was beta-lactams (ATC group J01C), with a range of 35.4% (Belarus) to 65.6% (Azerbaijan) of total J01 consumption. Cephalosporins (J01D) represented between 6.1% (Azerbaijan) and 30.3% (Turkey) of total consumption; quinolones (J01M) made up less than 0.1% of total consumption in Uzbekistan and 17% in the Republic of Moldova.

Cephalosporins and quinolones are broad-spectrum antibiotics and are considered second-line antibiotics in many prescribing guidelines. In the data reported here, the two groups combined represented between 10% (Azerbaijan) and 38% (Republic of Moldova) of total J01 consumption.

Choice of cephalosporins varied widely. Overall, consumption of fourth-generation agents was limited (mostly <0.1 DID). Consumption of first-generation agents varied from 8% (Turkey) to 80% (Serbia) of total cephalosporin consumption, and second-generation agents from very low consumption (<0.1 DID) in a number of settings to 54% of cephalosporin consumption (6.5 DID)

[1] All references to Kosovo in this summary should be understood as references to Kosovo in accordance with United Nations Security Council resolution 1244 (1999).

in Turkey. Third-generation agent consumption ranged from 16% (Serbia) to 83% (Tajikistan) of total cephalosporin consumption and represented more than 50% of total cephalosporin consumption in six of the 12 datasets.

Similarly, the relative consumption of amoxicillin and the broader-spectrum amoxicillin and clavulanic acid varied widely. Amoxicillin was the more consumed agent in most datasets – the exception was Turkey, where only 11% of consumption of these two agents was amoxicillin.

Estimates were derived for seven of the ESAC-Net quality indicators for antibiotic consumption. Variability in estimates of these indicators was considerable in both the WHO AMC Network and 2014 ESAC-Net analyses.

Conclusions

The results presented in this report document trends of AMC across parts of non-EU Europe. The notable feature of the cross-national comparisons is the wide variability of estimates. This is unlikely to be explained by different patterns or burden of disease alone. The reasons for such variability require further investigation and offer opportunities to develop interventions to promote more responsible use of antimicrobials.

The data sources used to provide consumption estimates have a number of limitations, and the results need to be interpreted in this light. Despite this, the levels of AMC reported, and in some cases the choices of antimicrobial agents used, confirm the need for action. A commitment to ongoing collection, analysis and use of consumption data is essential: it is a central element laid out in the Global Action Plan on antimicrobial resistance adopted during the Sixty-eighth World Health Assembly in May 2015.

1. INTRODUCTION

In September 2011 all 53 countries in the WHO European Region adopted the European strategic action plan on antibiotic resistance. This was developed in recognition of the following factors:

- in many countries in the Region antibiotic resistance had been neglected;
- no systematic surveillance of antibiotic use and resistance was in place;
- control efforts needed to be coordinated between the health and other relevant sectors;
- antibiotic resistance can spread internationally through travel and trade;
- international standards and mechanisms for sharing data and information were needed.

At the Sixty-eighth World Health Assembly held in May 2015, Member States adopted the Global Action Plan (WHO, 2015) on antimicrobial resistance and the resolution urged Member States to implement it, recognizing that this might need to be adapted to specific contexts and national priorities.

The Global Action Plan has five objectives:

- to improve awareness and understanding of antimicrobial resistance;
- to strengthen surveillance and research;
- to reduce the incidence of infection;
- **to optimize the use of antimicrobial medicines**; and
- to ensure sustainable investment in countering antimicrobial resistance.

Specifically related to objective 4, Member States were asked to provide "stewardship programmes that monitor and promote optimization of antimicrobial use at national and local levels in accordance with international standards in order to ensure the correct choice of medicine at the right dose on the basis of evidence". Thus, an important element of the Plan is monitoring the consumption of antimicrobial medicines. All countries have some data related to the import, procurement, distribution or clinical use of antimicrobials in their communities that can be used as the basis of stewardship and monitoring programmes.

Data on the consumption of antimicrobial medicines have a number of uses, including:

- relating exposure to antimicrobials to the development of antimicrobial resistance;
- identifying and providing an early warning of problems relating to changes in exposure and utilization and developing interventions to address problems identified;
- monitoring the outcomes of interventions aimed at changing exposure;
- assessing the quality of prescribing against practice guidelines;
- raising awareness in health professionals, consumers and policy-makers about the issues of antimicrobial resistance and the potential contribution of inappropriate use of antimicrobials in humans.

A considerable amount of work has already been undertaken in Europe to measure consumption of antimicrobials through two programmes undertaken by the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) and the WHO Regional Office for Europe.

2. THE WHO ANTIMICROBIAL MEDICINES CONSUMPTION (AMC) NETWORK

2.1 Background

The WHO AMC Network is an initiative of the WHO Regional Office for Europe and aims to support all countries and areas in the Region that are not part of ESAC-Net, coordinated by the European Centre for Disease Prevention and Control (ECDC) in the European Union (EU).

2.1.1 ESAC-Net

ESAC-Net is a Europe-wide network of national surveillance systems, providing European reference data on antimicrobial consumption. ESAC-Net collects and analyses data on antimicrobial consumption from EU, European Economic Area (EEA)[2] and European Free Trade Association (EFTA) countries, in both the community (primary care) and the hospital sectors.

The data collected by ESAC-Net are used to provide timely information and feedback to EU and EEA/EFTA countries on indicators of antimicrobial consumption. These indicators provide a basis for monitoring countries' progress towards prudent use of antimicrobials.

ESAC-Net publishes annual reports of antimicrobial consumption data, conveyed to ECDC using a standard reporting framework from the community and hospital sectors. In addition to the report, a selection of tables showing trends in consumption of antibacterials for systemic use in both sectors are available as separate downloadable files. ECDC also provides access to an interactive database on its website (ECDC, 2017a). This allows the display of selected data on antimicrobial consumption in different formats such as tables, maps and figures. It includes data on antimicrobial consumption in EU Member States and two EEA non-EU countries (Iceland and Norway) from 1997. This resource provides a powerful tool for examining changes in consumption over time and data at different levels of aggregation.

2.1.2 The WHO AMC Network

A pilot data collection project was undertaken in 2011, involving the Laboratory of Medical Microbiology of the University of Antwerp in Belgium, ECDC and the WHO Collaborating Centre for Drug Statistics Methodology, to monitor AMC at the national level in non-EU European Member

[2] The EEA unites the EU Member States and three of the four EFTA countries (Iceland, Liechtenstein and Norway) into an internal market governed by the same basic rules.

States. The project used the Anatomical Therapeutic Chemical (ATC) classification system and defined daily dose (DDD) methodology and the ESAC-Net data collection methods.

The Health Technologies and Pharmaceuticals Programme of the WHO Regional Office for Europe subsequently established a protocol for collection of AMC data that follows on from the pilot project work and the WHO AMC Network. This programme complements the work undertaken by ESAC-Net on AMC and by the WHO Regional Office for Europe with the Central Asian and Eastern European Surveillance of Antimicrobial Resistance (CAESAR) Network.

2.2 Objectives of the WHO AMC Network

The aim of the WHO AMC Network is to establish national surveillance systems for consumption of antimicrobial medicines. To complement the data obtained for the EU through ESAC-Net and enable comparison of data throughout the WHO European Region, the methodology for data collection used by the WHO AMC Network is closely aligned with that used by ECDC, to facilitate comparisons between EU and non-EU Member States in the Region. The data collected at the country and area level are shared with stakeholders and can be used to inform programmes and proposals for national policy actions to improve the responsible use of antimicrobials, as well as for cross-national comparisons. Fig.2.1 illustrates the scope of data collection by the WHO AMC Network in the Region.

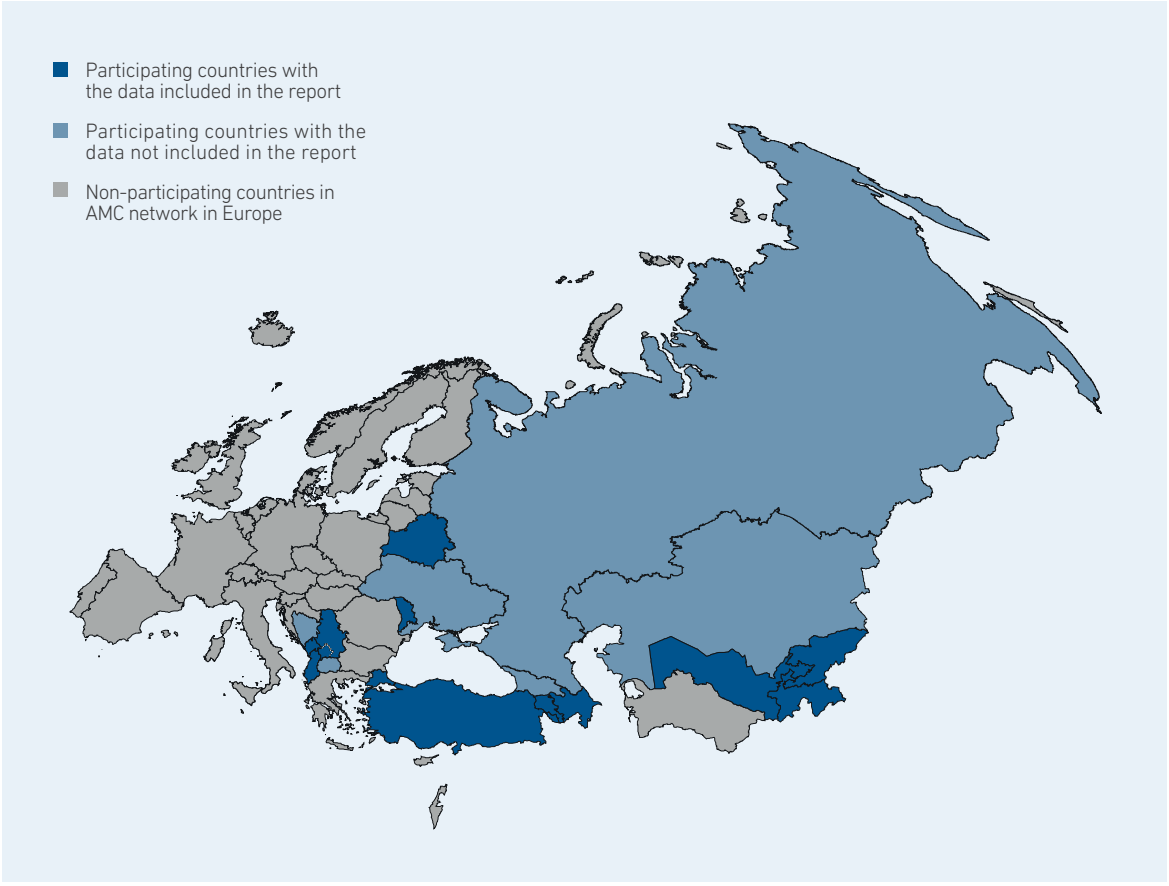

Fig. 2.1 Status of data reporting to the WHO AMC Network

2.3 Participating countries and areas

Albania, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Georgia, Kazakhstan, Kyrgyzstan, Montenegro, the Republic of Moldova, the Russian Federation, Serbia, Tajikistan, the former Yugoslav Republic of Macedonia, Turkey, Ukraine and Uzbekistan, as well as Kosovo,[3] are currently engaged in the WHO AMC Network. Between 2011 and 2014, all 18 contributed three or four years of antimicrobial consumption data to the Network. Of these, 11 countries and Kosovo[3] gave permission by the cut-off date of 30 November 2016 for the data to be published. Analyses for other Network members are shared with countries directly and may be included in future publications. Fig. 2.1 illustrates the scope of data collection by the WHO AMC Network in the Region.

[3] All references to Kosovo in this chapter should be understood as references to Kosovo in accordance with United Nations Security Council resolution 1244 (1999).

3. DATA COLLECTION AND ANALYSIS

3.1 Methodology

3.1.1 Definitions

For the purposes of this report, a distinction is made between consumption data and antimicrobial use data. This is done to recognize differences in the data sources and in the type of information that may be obtained from each approach.

- **Consumption data** are used to refer to estimates derived from aggregated data sources such as import or wholesaler data or aggregated health insurance data, where no information is available on the patients receiving the medicines or why the antimicrobials are used. These data sources provide a proxy estimate of use of antimicrobials. Consumption data may be presented as total consumption for a country or may be disaggregated by setting (community or hospital; public or private sectors).

- **Antimicrobial use data** are used to refer to estimates derived from patient-level data. These may allow disaggregation based on patient characteristics (such as gender or age) or indications for which the medicine is being used.

3.1.2 Measurements used

The WHO AMC Network uses the ATC classification system, and the most commonly used measurement metric is the number of DDDs. Details of both are provided in Annex 1.

The ATC classification system allows flexibility in reporting by medicine or groups of medicines. Medicines are classified in groups at five different levels. The majority of antimicrobial agents are classified in ATC main group J: anti-infectives for systemic use.

The DDD is the assumed average maintenance dose per day for a medicine used for its main indication in adults. The DDD is a technical unit of use and does not necessarily reflect the recommended or average prescribed daily dose. It is a useful metric that allows comparisons within and between countries.

3.1.3 Antimicrobials included in monitoring

The WHO AMC Network programme focuses only on antimicrobials for systemic use – it excludes topical antimicrobials. The core set of agents that all countries include in their monitoring is as follows:

- antibacterials (J01);
- antibiotics for alimentary tract and metabolism (A07AA);
- nitroimidazole derivatives against amoebiasis and other protozoal diseases (P01AB).

In addition, the WHO surveillance programme (WHO 2016) includes an optional list of antimicrobials that countries may include in their surveillance programmes according to local needs and resources:

- antimycotics for systemic use (J02);
- antifungals for systemic use (D01BA);
- antivirals for systemic use (J05);
- drugs for treatment of tuberculosis (J04A);
- antimalarials (P01B).

This report builds on the early experience of data collection at the country and area level. It provides an analysis of data collected between 2011 and 2014 and illustrates some cross-national comparisons for selected measures of AMC in 2014. The results it presents relate to analyses of antimicrobial agents in ATC group J01. Data relating to consumption of other antimicrobials – including antibiotics for alimentary tract and metabolism (A07AA), nitroimidazole derivatives against amoebiasis and other protozoal diseases (P01AB), antimycotics for systemic use (J02), antifungals for systemic use (D01BA), antivirals for systemic use (J05), drugs for treatment of tuberculosis (J04A) and antimalarials (P01B) – are also collected in some of the WHO AMC Network countries and areas but are not presented in this report. These additional analyses can be conducted at the country level and the results used to monitor antimicrobial consumption in these disease-specific areas.

3.1.4 Health care sectors monitored

In the majority of the countries and areas participating in the WHO AMC Network it is not possible to disaggregate data by sector (community or hospital; public or private), so total consumption data are reported in most cases.

3.2 Data collection

3.2.1 Sources of antimicrobial consumption data and progress with data collection 2011–2014

Most countries and areas participating in the WHO AMC Network use import data (from customs records and declaration forms) as the source of information on antimicrobial consumption. These are supplemented with sales records from market authorization holders or local manufacturing estimates where there is local pharmaceutical manufacturing. In some cases, data from wholesalers are used. Table 3.1 summarizes the years of data, health care sector coverage and data sources used in each of the settings included in this report.

Table 3.1 Sources of data used for consumption estimates (2011–2014)

Country or area	Years of data	Health care sector coverage	Data sources for consumption estimates
Albania	2011–2014	Total care	- Import records
Armenia	2011–2014	Total care	- Import records - Sales records from local manufacturers
Azerbaijan	2011–2014	Total care	- Import records
Belarus	2011–2014	Total care	- Import records - Sales records from local manufacturers
Kyrgyzstan	2011–2014	Total care	- Import records - Sales records from local manufacturers
Montenegro	2011–2014	Total care	- Import records
Republic of Moldova	2011–2014	Total care	- Import records - Sales records from local manufacturers
Serbia	2011–2014	Total care	- Sales records from marketing authorization holders
Tajikistan	2011–2014	Total care	- Import records - Certification records
Turkey	2011–2012 2013–2014	Outpatient Total care	- IMS Health - Wholesaler records from pharmaceutical track and trace system
Uzbekistan	2011–2014	Total care	- Import records
Kosovo (in accordance with Security Council resolution 1244 (1999))	2011–2014	Total care	- Import records

3.2.2 Data collection procedures

Data collection for the WHO AMC Network follows a standardized protocol and uses a common Excel template. Each year, the WHO regional team in Copenhagen launches a call for AMC data. The focal points fill in the template with AMC data (numbers of packages of each product imported or sold), the relevant product information and population data. Further details on data collection are provided in Annex 2.

All data in this report have been approved for publication by the ministry of health or relevant national authority.

3.3 Data analysis

3.3.1 Consumption estimates

Once the datasets are agreed, the WHO regional team analyses the data. The number of packages of each product is multiplied by the number of DDDs per package to calculate the total number of DDDs for each product. These are aggregated to give the total number of DDDs at the desired ATC code level.

Population-adjusted estimates of consumption are automatically calculated with embedded macros for calculation of consumption estimates in DDD per 1000 inhabitants per day (DID). Further details of population estimates are provided in Annex 2.

3.3.2 Metrics reported

The use of the ATC classification permits analyses at five different levels – from main class (level 1) to individual medicine (level 5) (see Annex 1). The AMC data for ATC category J01 are analysed to give both country- or area-specific trends in antimicrobial consumption and trends and differences in cross-national comparisons.

This report focuses on four types of key measure used to examine trends over time within countries and areas and in cross-national comparisons (Table 3.2):

- volume of consumption measures, reported as numbers of DID;
- relative consumption measures, expressed as a percentage of total consumption of a group of antimicrobials;
- the agents consumed, reflecting the choice of specific antimicrobial agents within a class and allowing more focused assessment of whether the choices align with recommended best practices and clinical practice guidelines;
- utilization of the 10 most consumed agents.

Table 3.2 Metrics used in analyses over time and in cross-national comparisons

Category	Unit
Estimates of volumes of consumption of antibacterials for systemic use (J01)	
Total consumption of J01 antibacterials by route of administration	DID[a]
Total consumption of J01 antibacterials by pharmacological subgroup: - tetracyclines (J01A) - amphenicols (J01B) - beta-lactams (J01C) - cephalosporins (J01D) - sulfonamides and trimethoprim (J01E) - macrolides, lincosamides and streptogramins (J01F) - quinolone antibacterials (J01M) - other J01 antibacterials (J01G, J01R, J01X)	DID
Relative consumption of J01 antibacterials by subgroup	
Relative consumption of J01 antibacterials by pharmacological subgroup	%
Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials	%
Relative consumption by choice of agent	
Relative consumption of agents of cephalosporins by generation	%
Relative consumption of cephalosporins by generation: - choice of first-generation cephalosporins (J01DB) - choice of second-generation cephalosporins (J01DC) - choice of third-generation cephalosporins (J01DD) - choice of fourth-generation cephalosporins (J01DE)	%
Relative consumption of agents within fluoroquinolones (J01MA)	%
Relative consumption of amoxicillin and amoxicillin and clavulanic acid	%
The 10 most consumed agents	
The 10 most consumed agents – oral formulation	DID
The 10 most consumed agents – parenteral formulation	DID

[a] DID: DDD/1000 inhabitants per day.

3.3.2.1 Route of administration

Oral administration is generally regarded as the most acceptable and economical method of administration of antimicrobials. Hospitalized patients initially on intravenous antibiotics can often be safely switched to an oral equivalent once they are clinically stable. Oral medication is associated with fewer complications, lower health care costs and earlier hospital discharge. Nevertheless, it must be recognized that there may also be cultural and medical practice traditions that favour use of parenteral formulations in some settings.

This report includes analyses of use of oral and parenteral formulations for J01 medicines. Where use of parenteral formulations is comparatively high, there may be opportunities to increase use of oral formulations without loss of clinical efficacy.

3.3.2.2 Total consumption in DDD per 1000 inhabitants per day

The DDD per 1000 inhabitants per day (abbreviated to DID) is the most commonly reported metric of antimicrobial consumption and the most frequently used measure in cross-national comparisons (see Chapter 16).

It should be noted that only medicines assigned an ATC code and DDD are included in the analyses reported here. In several countries in the WHO AMC Network, a number of medicines without such codes are consumed by the population. Exclusion of these medicines means that data are missing in the numerator for the calculation, and the resulting DID estimates will underestimate total antimicrobial consumption in the country.

3.3.2.3 Quinolones and cephalosporins

Quinolones and cephalosporins are broad-spectrum antibiotics and are considered second-line antibiotics in most prescribing guidelines (Adriaenssens et al., 2011a). Thus, their use should be restricted to ensure availability as second-line therapy, should first-line antibiotics fail.

Guidance from authorities such as Public Health England (2016) suggests that simple generic antibiotics should be used if possible when antibiotics are necessary. Broad-spectrum antibiotics (for example, amoxicillin and clavulanic acid, quinolones and cephalosporins) need to be reserved to treat resistant disease. They should generally be used only when narrow-spectrum antibiotics are ineffective because they increase the risk of methicillin-resistant *Staphylococcus aureus*, *Clostridium difficile* and resistant urinary tract infections.

Public Health England also notes that although identifying the cephalosporin and quinolone classes as high risk may have been an important control measure in reducing the risk of *Clostridium difficile* infection, an unintended consequence may have been a recent increase in clinically inappropriate prescribing of co-amoxiclav and other broad-spectrum antibiotics, such as piperacillin-tazobactam. These alternative antibiotics have a very limited set of recommended clinical indications.

WHO (2012) identifies fluoroquinolones, third- and fourth-generation cephalosporins, macrolides and glycopeptides as being of highest priority for risk management to ensure that critically important antimicrobials are used prudently both in human and veterinary medicine. While there is no optimal level of prescribing of quinolones and cephalosporins, their volume as a proportion of all antibiotic prescribing has been validated as a marker of quality in the primary care setting (Adriaenssens et al., 2011b) – see Annex 2.

3.3.2.4 Fluoroquinolones

Fluoroquinolones (J01MA) are the most widely used agents within the quinolone antibacterials (J01M) group. Public Health England identifies the prescribing of fluoroquinolones such as ciprofloxacin and ofloxacin in general practice as a cause for concern. Resistance to quinolones has increased at a considerable rate (for example, quinolone-resistant *Neisseria gonorrhoeae*) and is usually high level, affecting all the quinolones. Public Health England guidance on managing common infections recommends that quinolones are used as first-line treatment only for acute pyelonephritis, acute prostatitis, epididymitis and pelvic inflammatory disease. The guidance suggests that fluoroquinolones should be used in lower respiratory tract infections only when there is proven resistance to other antibiotics.

3.3.2.5 Cephalosporins

Third- and fourth-generation cephalosporins have a broader spectrum of activity than first- and second-generation agents, with enhanced coverage of both Gram-positive and Gram-negative organisms.

3.3.2.6 Amoxicillin, amoxicillin and clavulanic acid

The addition of clavulanic acid to amoxicillin extends the spectrum of activity of amoxicillin against beta-lactamase-producing bacteria. Amoxicillin and clavulanic acid is recommended as second-line treatment in many treatment guidelines.

Further details of measurement metrics and quality indicators for antimicrobial consumption are provided in Annex 3.

3.4 Data interpretation

The goal of the AMC surveillance data collected and presented in this report is to provide a description of consumption of the antimicrobials in class J01. For a correct assessment of the magnitude and trends of antimicrobial consumption in the country or area and to allow cross-national comparison of results, the data are required to be both valid and reliable.

The validity and reliability of data may be compromised at different points, however. These include:

- incomplete registration of antimicrobial products in circulation in the country
- incomplete capture and reporting of data
- double counting of medicines from different data sources
- errors in data entry that were not identified during data validation
- data excluded from calculations where no ATC or DDD is assigned for the medicine.

Together these errors will affect the absolute values for antimicrobial consumption (measured in DID).

Incomplete data capture may occur when not all wholesalers provide data on products sold. Sales data from local manufacturers need to distinguish between medicines for local consumption and medicines exported.

In a number of countries and areas participating in the WHO AMC Network, no ATC or DDD is assigned to a considerable number of products. Consumption of these medicines is excluded from

the analyses reported here, meaning that total consumption estimates presented underestimate actual consumption of antibacterials.

The WHO Regional Office for Europe is working with participants in the WHO AMC Network and the WHO Collaborating Centre for Drug Statistics Methodology to identify products without codes and to resolve these for future analyses.

3.4.1 Import data

A particular issue with data derived from importation records is that the estimates will be affected by the cycles of procurement and delivery. For example, if tenders apply for a two-year period, it is unlikely that deliveries will occur in similar quantities and at regular intervals during that time. Receipt of two or more deliveries in one year may be followed by importation of smaller quantities in the next. This may give rise to fluctuations in estimates of consumption that do not relate to use of antibacterials by patients and health care facilities.

Import cycles are also likely to mean that different products are received at different times. Thus, relative use estimates may also be affected. Notwithstanding these limitations, it is reasonable to assume that over a longer period the relative use estimates will stabilize and more closely reflect the relative consumption of different antibacterial agents. Consequently, trends over time need to be interpreted carefully. In general, import data should not be used to make comparisons on monthly or quarterly consumption.

The analyses in this report provide annual consumption estimates. The fluctuations in total consumption estimates from a number of countries, however, suggest that import cycles may contribute in part to the patterns of consumption shown.

3.4.2 Information value

The data presented may not yet be optimal, or systemic issues may lead to biased estimates, but recognizing these limitations may encourage WHO AMC Network countries and areas to consider using different data sources, such as wholesaler rather than import data. Later, as information systems develop, it may be possible to derive consumption estimates from reimbursement records from health insurance agencies and e-prescribing platforms.

Even with the data limitations, the variability of consumption patterns within and between countries provides a basis for further investigation to better understand how antibacterials are used in practice. The consumption data need to be interpreted with an understanding of the local context, taking account of changes in regulations (including enforcement of prescription-only status), data sources, resistance patterns and the potential impact of interventions to change practices.

4. ALBANIA

4.1 Data sources and years of data collection

Albania provided data for each of the four years of data collection (2011–2014). The main sources were import records provided by the drug agency (Table 4.1).

Table 4.1 Sources of data used for consumption estimates (2011–2014)

Year	Health care sector coverage	Data type	Data source (consumption)	Population	Data source (population)
2011	Total care	Import records	Drug agency	2 904 780	World Bank
2012	Total care	Import records	Drug agency	2 900 489	World Bank
2013	Total care	Import records	Drug agency	2 897 366	World Bank
2014	Total care	Import records	Drug agency	2 893 654	World Bank

4.2 Estimates of volumes of consumption of antibacterials for systemic use (J01)

Total consumption of antibacterials for systemic use (ATC class J01) is examined by route of administration (oral and parenteral formulations) and by pharmacological subgroup.

4.2.1 Total consumption of J01 antibacterials by route of administration

The consumption of oral and parenteral (injectable) formulations of J01 antibacterials is shown in Fig. 4.1 and summarized in Table 4.2 as DDD/1000 inhabitants per day (DID).

The import data show some fluctuations in total consumption over time (25.1 DID in 2011 to 22.7 DID in 2014); however, this might be explained in part by import cycles for these medicines.

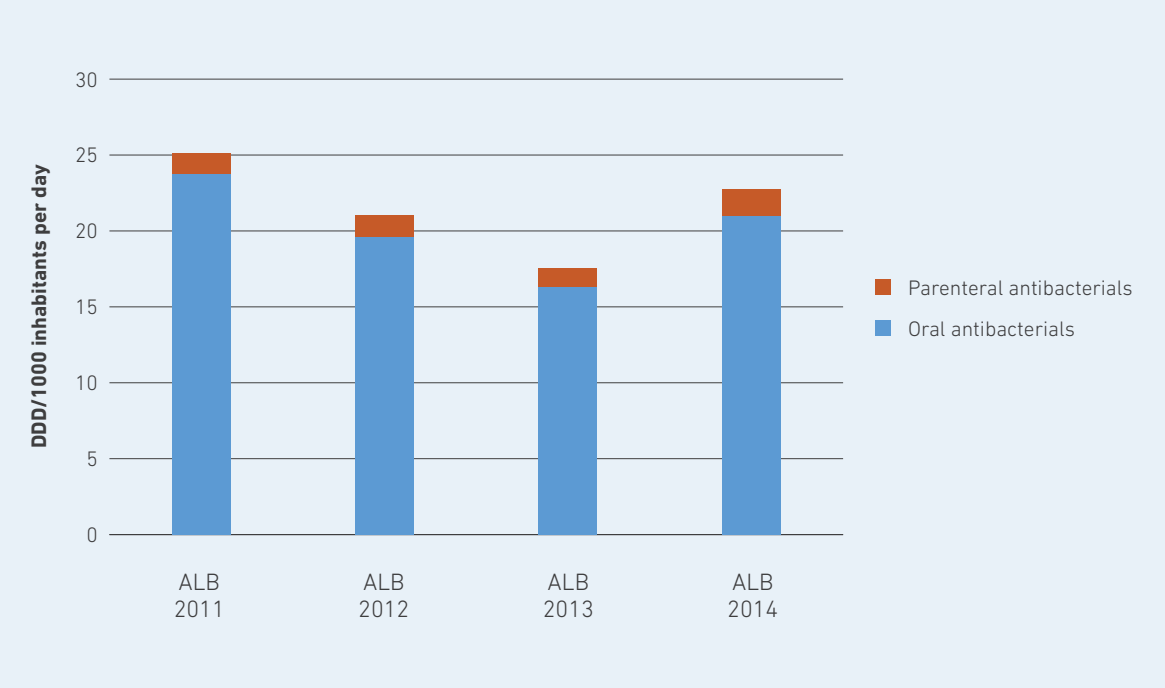

Fig. 4.1 Total consumption of J01 antibacterials by route of administration

DDD: defined daily dose.

The relative consumption of parenteral antibacterials remained reasonably stable at around 7-8% of total J01 consumption (Table 4.2).

Table 4.2 Total consumption of J01 antibacterials by route of administration

Route of administration	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Oral J01	23.8 (95)	19.6 (93)	16.3 (93)	21 (92)
Parenteral J01	1.4 (5)	1.5 (7)	1.3 (7)	1.8 (8)
Total	**25.1**	**21.1**	**17.5**	**22.7**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

4.2.2 Total consumption of J01 antibacterials by pharmacological subgroup

The consumption of J01 antibacterials by pharmacological subgroup is shown in Fig. 4.2 and summarized in Table 4.3.

Numerically, the largest changes in consumption of pharmacological subgroups occurred in the tetracyclines subgroup (J01A), which decreased from 7.8 DID in 2011 to 3.6 DID in 2014. The highest levels of consumption were in beta-lactams (J01C), at 8.6 DID in 2011 and 9.9 DID in 2014. There were trends towards increasing use of beta-lactams (J01C), cephalosporins (J01D) and macrolides, lincosamides and streptogramins (J01F) between 2011 and 2014.

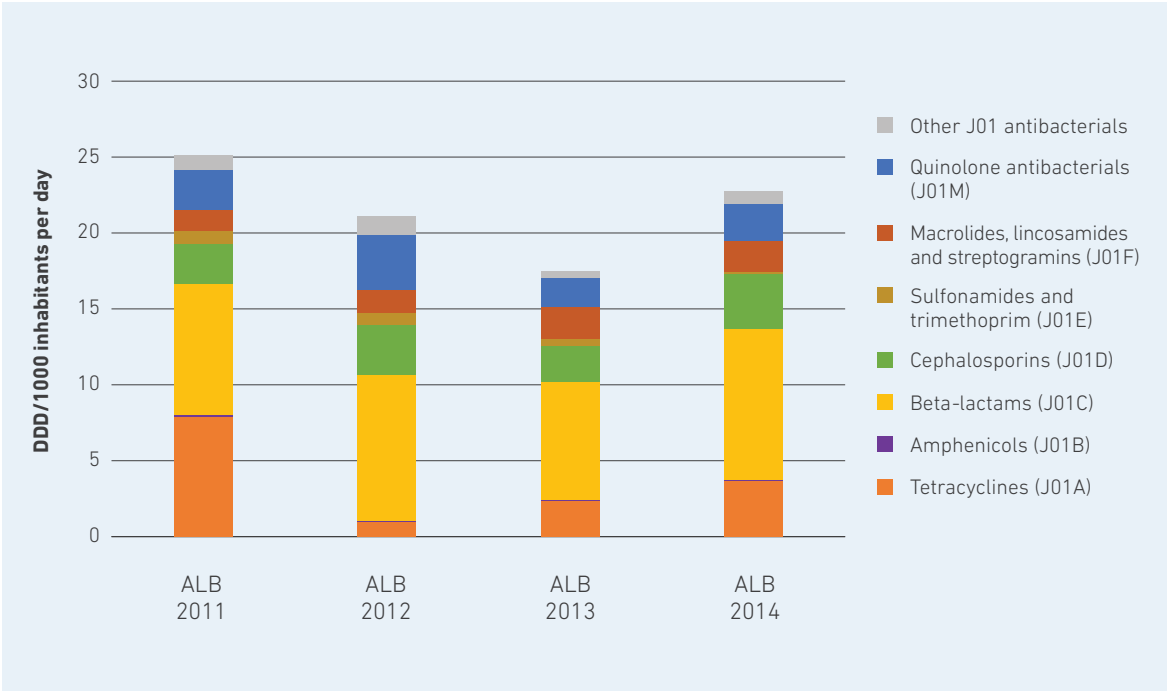

Fig. 4.2 Total consumption of J01 antibacterials by pharmacological subgroup

DDD: defined daily dose.

Table 4.3 Total consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	DDD/1000 inhabitants per day[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	7.8	0.9	2.3	3.6
Amphenicols (J01B)	0.2	0.1	0.1	0.1
Beta-lactams (J01C)	8.6	9.6	7.8	9.9
Cephalosporins (J01D)	2.7	3.3	2.4	3.6
Sulfonamides and trimethoprim (J01E)	0.9	0.8	0.5	0.2
Macrolides, lincosamides and streptogramins (J01F)	1.3	1.5	2.1	2.0
Quinolone antibacterials (J01M)	2.7	3.6	1.9	2.4
Other J01 antibacterials (J01G, J01R, J01X)	1.0	1.2	0.5	0.8
Total[b]	**25.1**	**21.1**	**17.5**	**22.7**

[a] DDD: daily defined dose. [b] Total amounts may vary slightly owing to rounding.

4.3 Relative consumption of J01 antibacterials by subgroup

4.3.1 Relative consumption of J01 antibacterials by pharmacological subgroup

The relative consumption of pharmacological subgroups measured as a proportion of total J01 antibacterials is shown in Fig. 4.3 and summarized in Table 4.4.

There has been a decline in consumption of tetracylines (J01A) over time. While it is a quantitatively a smaller decline, consumption of sulfonamides and trimethoprim (J01E) also decreased over time (from 3.5% of total J01 consumption in 2011 to 0.7% in 2014) (Table 4.4).

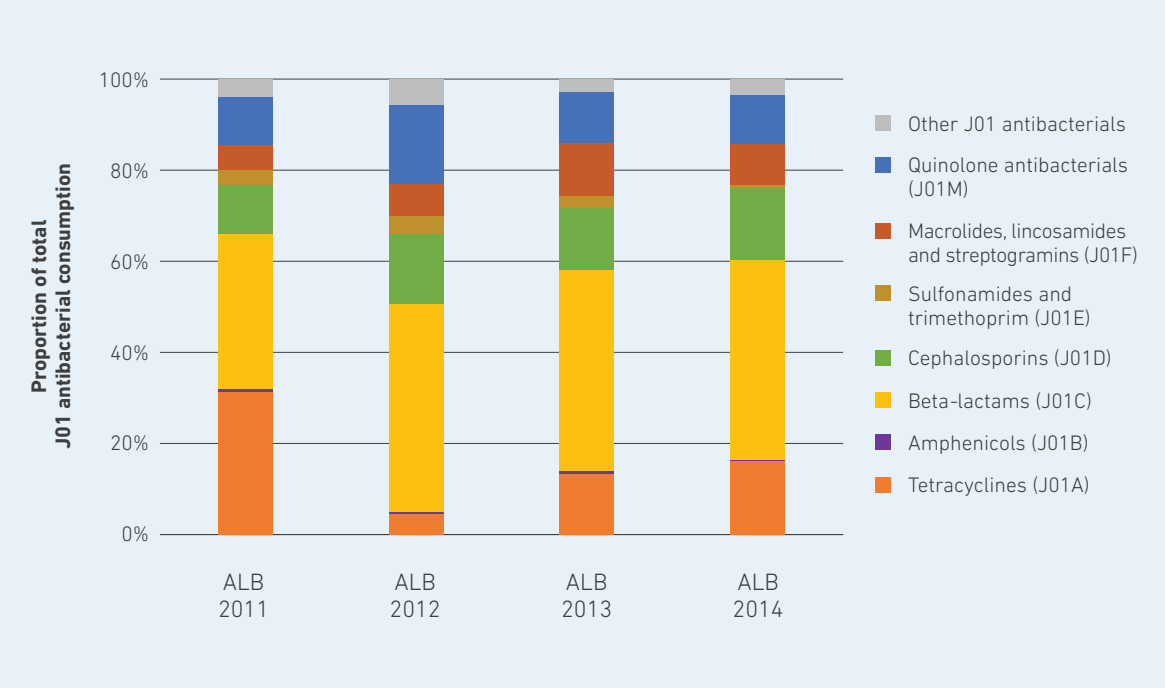

Fig. 4.3 Relative consumption of J01 antibacterials by pharmacological subgroup

Table 4.4 Relative consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	Consumption as proportion of total J01 consumption (%)[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	31.2	4.5	13.2	16.0
Amphenicols (J01B)	0.7	0.3	0.6	0.4
Beta-lactams (J01C)	34.2	45.7	44.2	43.7
Cephalosporins (J01D)	10.6	15.5	13.5	15.9
Sulfonamides and trimethoprim (J01E)	3.5	3.9	2.7	0.7
Macrolides, lincosamides and streptogramins (J01F)	5.4	7.1	11.8	9.0
Quinolone antibacterials (J01M)	10.7	17.3	11.0	10.7
Other J01 antibacterials (J01G, J01R, J01X)	3.9	5.7	2.9	3.6

[a] Total percentages may vary slightly owing to rounding.

Beta-lactams (J01C) was the most consumed pharmacological subgroup in 2011–2014, at 43.7% of total J01 consumption in 2014, followed by the tetracyclines (J01A), at 16%, cephalosporins (J01D), at 15.9%, and quinolone antibacterials (J01M), at 10.7%.

4.3.2 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Cephalosporins and quinolones are broad-spectrum antibiotics and are considered second-line antibiotics in most prescribing guidelines. Generally, it is recommended that their use should be restricted to ensure availability as second-line therapy, should first-line antibiotics fail.

The relative consumption of cephalosporins and quinolones measured as a proportion of total J01 antibacterials is shown in Fig. 4.4 and summarized in Table 4.5.

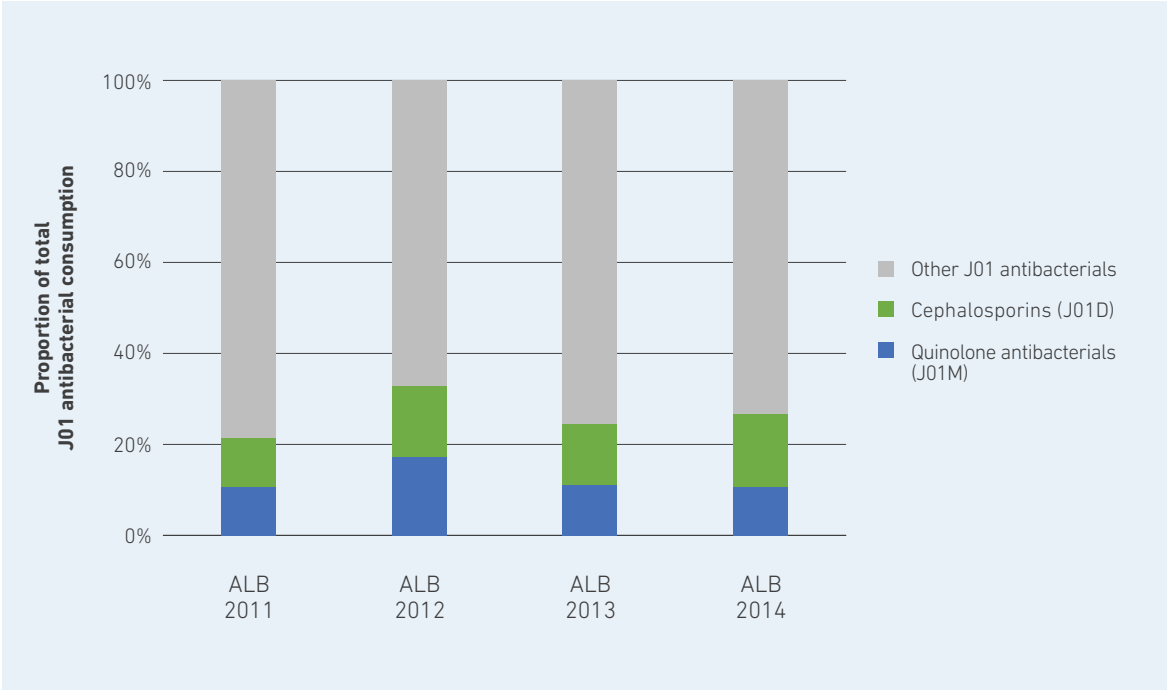

Fig. 4.4 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Consumption of quinolone antibacterials was reasonably stable in 2011–2014 (at around 11% of total J01 consumption), while the data suggest an increase in consumption of cephalosporins during the period. Together, the two groups constituted 27% of J01 antibacterial consumption in 2014 (Table 4.5).

Table 4.5 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Class of antibacterial agents	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Quinolone antibacterials (J01M)	2.7 (11)	3.6 (17)	1.9 (11)	2.4 (11)
Cephalosporins (J01D)	2.7 (11)	3.3 (16)	2.4 (13)	3.6 (16)
Other J01 antibacterials	19.8 (79)	14.1 (67)	13.2 (75)	16.7 (73)
Total	**25.1**	**21.1**	**17.5**	**22.7**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

4.4 Relative consumption by choice of agent

4.4.1 Relative consumption of cephalosporins by generation

Third- and fourth-generation cephalosporins have a broader spectrum of activity than first- and second-generation agents, with enhanced coverage of both Gram-positive and Gram-negative

organisms. WHO (2012) has identified third- and fourth-generation cephalosporins as some of the agents of highest priority for risk management to ensure that critically important antimicrobials are used prudently both in human and veterinary medicine.

The relative consumption of first-, second-, third- and fourth-generation cephalosporins in 2011–2014 is shown in Fig. 4.5 and summarized in Table 4.6.

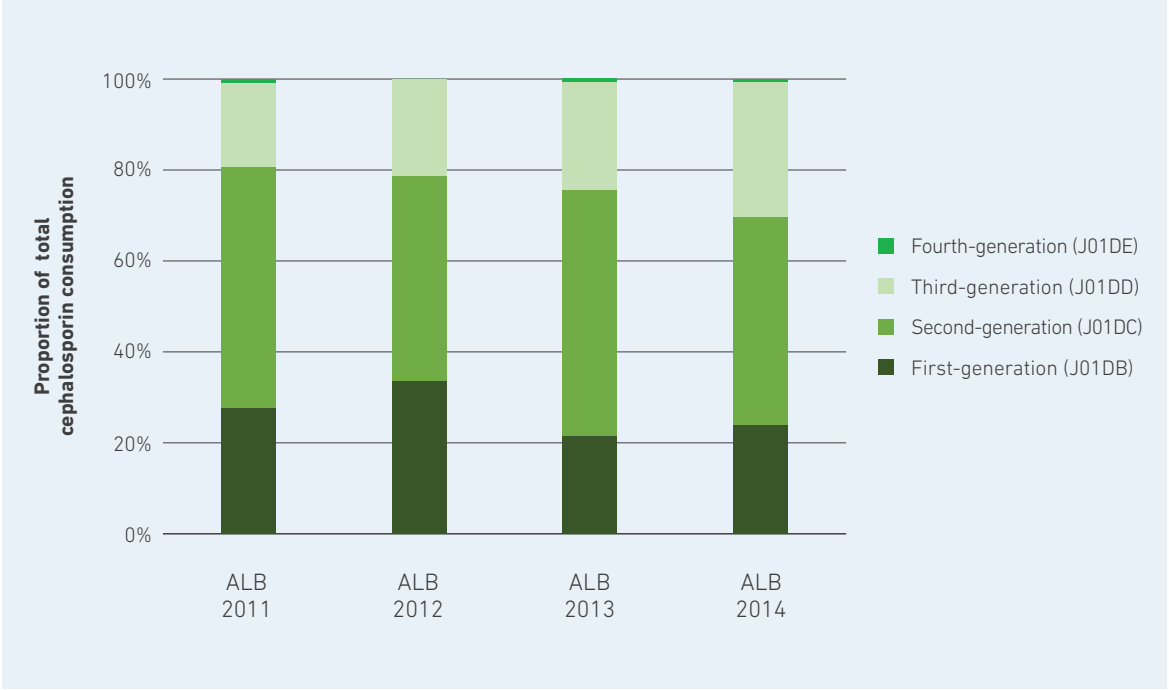

Fig. 4.5 Relative consumption of cephalosporins by generation

Consumption of fourth-generation cephalosporins was very limited (<0.1 DID) during 2011–2014, but consumption of third-generation agents increased (from 19% in 2011 to 30% in 2014) and consumption of first- and second-generation agents decreased from 81% to 70% of total cephalosporin use across the period (Table 4.6).

Table 4.6 Relative consumption of cephalosporins by generation

Generation	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
First-generation (J01DB)	0.7 (28)	1.1 (34)	0.5 (21)	0.9 (24)
Second-generation (J01DC)	1.4 (53)	1.5 (45)	1.3 (54)	1.7 (46)
Third-generation (J01DD)	0.5 (19)	0.7 (21)	0.6 (24)	1.1 (30)
Fourth-generation (J01DE)	<0.1	<0.1	<0.1	<0.1
Total	**2.7**	**3.3**	**2.4**	**3.6**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

4.4.1.1 Choice of first-generation cephalosporins (J01DB)

Table 4.7 summarizes the pattern of consumption of first-generation cephalosporins in 2011–2014. Cefalexin and cefazolin were those most consumed agents.

Table 4.7 Relative consumption of agents within first-generation cephalosporins (J01DB)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefalexin	0.5 (74)	0.8 (75)	0.4 (71)	0.4 (47)
Cefazolin	0.2 (26)	0.3 (25)	0.1 (28)	0.4 (53)
Cefradine	–	–	<0.1	<0.1
Total	**0.7**	**1.1**	**0.5**	**0.9**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

4.4.1.2 Choice of second-generation cephalosporins (J01DC)

Table 4.8 summarizes the pattern of consumption of second-generation cephalosporins in 2011–2014. Cefuroxime and cefaclor were those most consumed.

Table 4.8 Relative consumption of agents within second-generation cephalosporins (J01DC)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefuroxime	0.6 (46)	0.6 (40)	0.8 (64)	1.1 (64)
Cefaclor	0.7 (52)	0.8 (58)	0.4 (33)	0.5 (33)
Cefonicide	<0.1	<0.1	<0.1	–
Cefprozil	<0.1	<0.1	<0.1	<0.1
Total	**1.4**	**1.5**	**1.3**	**1.7**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

4.4.1.3 Choice of third-generation cephalosporins (J01DD)

Table 4.9 summarizes the pattern of consumption of third-generation cephalosporins in 2011–2014. Ceftriaxone and cefixime were those most consumed.

Table 4.9 Relative consumption of agents within third-generation cephalosporins (J01DD)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefotaxime	<0.1	<0.1	<0.1	<0.1
Ceftazidime	<0.1	<0.1	<0.1	<0.1
Ceftriaxone	0.3 (55)	0.3 (44)	0.3 (48)	0.6 (52)
Cefixime	0.2 (40)	0.3 (50)	0.2 (42)	0.4 (38)
Cefpodoxime	–	–	–	<0.1
Cefdinir	–	–	<0.1	<0.1
Total	**0.5**	**0.7**	**0.6**	**1.1**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

4.4.1.4 Choice of fourth-generation cephalosporins (J01DE)

Consumption of fourth-generation cephalosporins was low during 2011–2014, with cefpirome consumed in small amounts.

4.4.2 Relative consumption of agents within fluoroquinolones (J01MA)

Quinolone antibacterials comprised around 11% of consumption of J01 antibacterials during 2011–2014 (see Table 4.4). Around 90% of quinolone consumption was from the fluoroquinolone category (J01MA). The most consumed agents were ciprofloxacin and levofloxacin (Table 4.10).

Table 4.10 Relative consumption of agents within fluoroquinolones (J01MA)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Ciprofloxacin	1.3 (52)	1.9 (53)	1.6 (86)	1.8 (79)
Norfloxacin	0.2 (7)	0.3 (9)	<0.1	0.1 (5)
Rufloxacin	<0.1	<0.1	<0.1	–
Levofloxacin	0.1 (6)	0.1 (4)	0.1 (8)	0.3 (15)
Moxifloxacin	0.9 (36)	1.2 (34)	<0.1	<0.1
Total	**2.4**	**3.5**	**1.8**	**2.3**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

4.4.3 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

The addition of clavulanic acid to amoxicillin extends the spectrum of activity of amoxicillin against beta-lactamase-producing bacteria. Amoxicillin and clavulanic acid is recommended as second-line treatment in many treatment guidelines.

Table 4.11 summarizes the relative consumption of amoxicillin and broader-spectrum amoxicillin and clavulanic acid. Amoxicillin was the more consumed agent in all years reported.

Table 4.11 Relative consumption of amoxicillin and amoxicillin and clavulanic acid

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Amoxicillin (J01CA04)	5.4 (70)	5.9 (64)	3.7 (53)	5.8 (63)
Amoxicillin and clavulanic acid (J01CR02)	2.4 (30)	3.3 (36)	3.3 (47)	3.4 (37)
Total	**7.8**	**9.1**	**7.0**	**9.1**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

4.5 The 10 most consumed agents

While the number of J01 antibacterial agents available is large, there is considerable evidence from ESAC-Net and other analyses that consumption tends to be concentrated in a relatively small number.

4.5.1 The 10 most consumed agents – oral formulation

Table 4.12 summarizes consumption of the oral agents that comprise the 10 most consumed in 2014. Seven agents (amoxicillin, amoxicillin and enzyme inhibitor, tetracycline, ciprofloxacin, doxycycline, azithromycin and cefuroxime) account for just over 76% of consumption.

Table 4.12 The 10 most consumed agents – oral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Amoxicillin	5.78	5.78	5.78	5.78	5.78	5.78	5.78	5.78	5.78	5.78
Amoxicillin and enzyme inhibitor	3.36	3.36	3.36	3.36	3.36	3.36	3.36	3.36	3.36	
Tetracycline	2.08	2.08	2.08	2.08	2.08	2.08	2.08	2.08		
Ciprofloxacin	1.72	1.72	1.72	1.72	1.72	1.72	1.72			
Doxycycline	1.09	1.09	1.09	1.09	1.09	1.09				
Azithromycin	1.00	1.00	1.00	1.00	1.00					
Cefuroxime	0.98	0.98	0.98	0.98						
Clarithromycin	0.78	0.78	0.78							
Ampicillin	0.60	0.60								
Cefaclor	0.54									
Total consumption for this group of agents	**17.93**	**17.39**	**16.79**	**16.01**	**15.04**	**14.03**	**12.94**	**11.22**	**9.14**	**5.78**
Total consumption for all oral J01 antibacterials	**20.96**	**20.96**	**20.96**	**20.96**	**20.96**	**20.96**	**20.96**	**20.96**	**20.96**	**20.96**
Proportion (%) of total consumption for oral J01 antibacterials	**85.6%**	**83.0%**	**80.1%**	**76.4%**	**71.7%**	**67.0%**	**61.8%**	**53.5%**	**43.6%**	**27.6%**

[a] DDD: daily defined dose.

4.5.2 The 10 most consumed agents – parenteral formulation

Table 4.13 summarizes consumption of the 10 most consumed parenteral agents in 2014. Four of these (ceftriaxone, cefazolin, gentamicin and ciprofloxacin) account for just over 77% of consumption.

Table 4.13 The 10 most consumed agents – parenteral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Ceftriaxone	0.55	0.55	0.55	0.55	0.55	0.55	0.55	0.55	0.55	0.55
Cefazolin	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45	
Gentamicin	0.27	0.27	0.27	0.27	0.27	0.27	0.27	0.27		
Ciprofloxacin	0.12	0.12	0.12	0.12	0.12	0.12	0.12			
Ampicillin	0.09	0.09	0.09	0.09	0.09	0.09				
Cefuroxime	0.08	0.08	0.08	0.08	0.08					
Metronidazole	0.07	0.07	0.07	0.07						
Amikacin	0.04	0.04	0.04							
Cefotaxime	0.04	0.04								
Cefepime	0.02									
Total consumption for this group of agents	**1.73**	**1.71**	**1.67**	**1.63**	**1.56**	**1.48**	**1.39**	**1.27**	**1.00**	**0.55**
Total consumption for all parental J01 antibacterials	**1.79**	**1.79**	**1.79**	**1.79**	**1.79**	**1.79**	**1.79**	**1.79**	**1.79**	**1.79**
Proportion (%) of total consumption for parental J01 antibacterials	**97.0%**	**95.8%**	**93.5%**	**91.1%**	**87.4%**	**82.8%**	**77.7%**	**71.2%**	**56.0%**	**30.8%**

[a] DDD: daily defined dose.

4.6 Comments

The analyses presented in this chapter are based on import records, and the results suggest that import cycles may have an impact on the estimates and explain (in part) the fluctuations between years.

Consideration could be given to exploring the use of additional data sources, such as wholesaler data, to create more robust consumption estimates, including disaggregation to community and hospital sectors. A more detailed understanding of the patterns of antimicrobial consumption would identify areas for further investigation and allow development of targeted interventions to address potential problems identified in the consumption of antibacterials.

5. ARMENIA

5.1 Data sources and years of data collection

Armenia provided data for each of the four years of data collection (2011–2014). The main sources were import records provided by the drug agency and information provided by local pharmaceutical manufacturers (Table 5.1). Further information on the estimates provided by local manufacturers was not available.

Table 5.1 Sources of data used for consumption estimates (2011–2014)

Year	Health care sector coverage	Data type	Data source (consumption)	Population	Data source (population)
2011	Total care	Import records Sales records	Drug agency Local manufacturers	2 964 120	World Bank
2012	Total care	Import records Sales records	Drug agency Local manufacturers	2 969 081	World Bank
2013	Total care	Import records Sales records	Drug agency Local manufacturers	2 976 566	World Bank
2014	Total care	Import records Sales records	Drug agency Local manufacturers	3 006 154	World Bank

5.2 Estimates of volumes of consumption of antibacterials for systemic use (J01)

Total consumption of antibacterials for systemic use (ATC class J01) is examined by route of administration (oral and parenteral formulations) and by pharmacological subgroup.

5.2.1 Total consumption of J01 antibacterials by route of administration

The consumption of oral and parenteral (injectable) formulations of J01 antibacterials is shown in Fig. 5.1 and summarized in Table 5.2 as DDD/1000 inhabitants per day (DID).

The data show some fluctuations in total consumption of J01 antibacterials over time, with the highest levels in 2011 (15.9 DID), a fall in 2012, then increasing consumption estimates between

2012 and 2014. It is unclear whether the results relate to a true reduction in consumption in 2012, changes in data sources or the influence of medicine import cycles. Further investigation is required to explain these observations.

Fig. 5.1 Total consumption of J01 antibacterials by route of administration

DDD: defined daily dose.

The relative consumption of parenteral antibacterials remained reasonably stable at around 10–12% of total J01 consumption (Table 5.2).

Table 5.2 Total consumption of J01 antibacterials by route of administration

Route of administration	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Oral J01	14.2 (89)	10 (88)	12.2 (88)	12.9 (90)
Parenteral J01	1.7 (11)	1.4 (12)	1.7 (12)	1.5 (10)
Total	**15.9**	**11.4**	**13.9**	**14.4**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

5.2.2 Total consumption of J01 antibacterials by pharmacological subgroup

The consumption of J01 antibacterials by pharmacological subgroup is shown in Fig. 5.2 and summarized in Table 5.3.

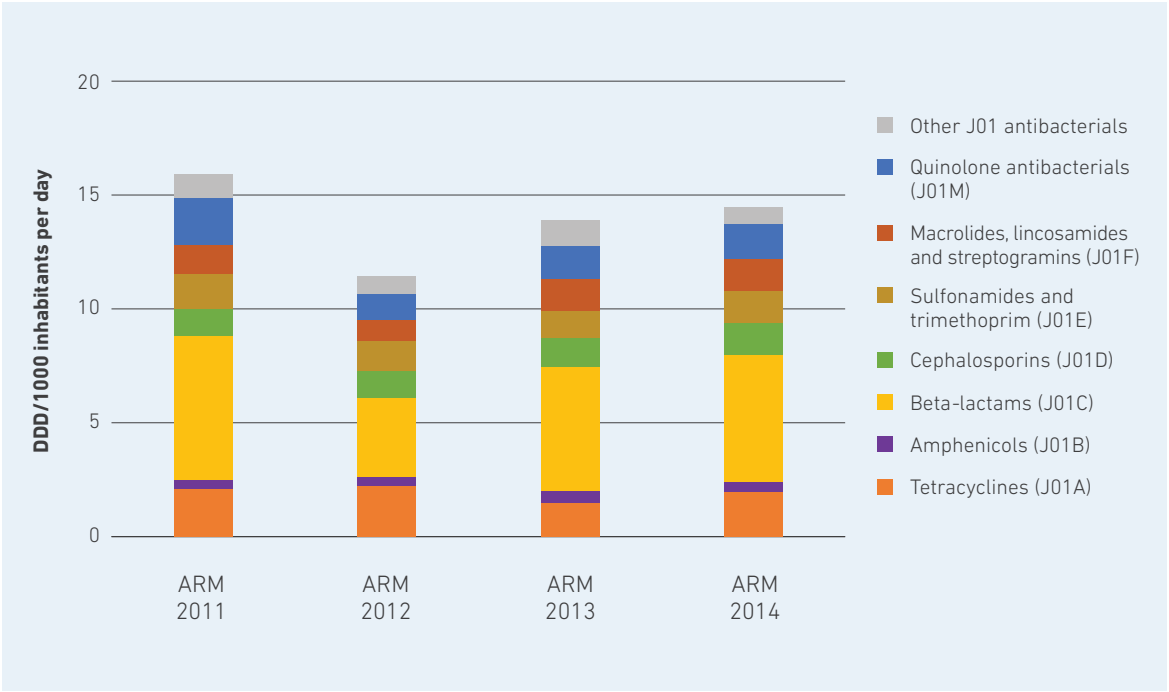

Fig. 5.2 Total consumption of J01 antibacterials by pharmacological subgroup

DDD: defined daily dose.

The highest levels of consumption were in beta-lactams (J01C), at 6.3 DID in 2011 and 5.6 DID in 2014, and tetracyclines (J01A), at 2.1 DID in 2011 and 2 DID in 2014 (Table 5.3).

Table 5.3 Total consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	DDD/1000 inhabitants per day[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	2.1	2.2	1.5	2.0
Amphenicols (J01B)	0.4	0.4	0.5	0.4
Beta-lactams (J01C)	6.3	3.5	5.5	5.6
Cephalosporins (J01D)	1.2	1.2	1.2	1.4
Sulfonamides and trimethoprim (J01E)	1.5	1.3	1.2	1.4
Macrolides, lincosamides and streptogramins (J01F)	1.3	0.9	1.4	1.4
Quinolone antibacterials (J01M)	2.0	1.1	1.5	1.5
Other J01 antibacterials (J01G, J01R, J01X)	1.1	0.8	1.1	0.7
Total[b]	**15.9**	**11.4**	**13.9**	**14.4**

[a] DDD: daily defined dose. [b] Total amounts may vary slightly owing to rounding.

5.3 Relative consumption of J01 antibacterials by subgroup

5.3.1 Relative consumption of J01 antibacterials by pharmacological subgroup

The relative consumption of pharmacological subgroups measured as a proportion of total J01 antibacterials is shown in Fig. 5.3 and summarized in Table 5.4.

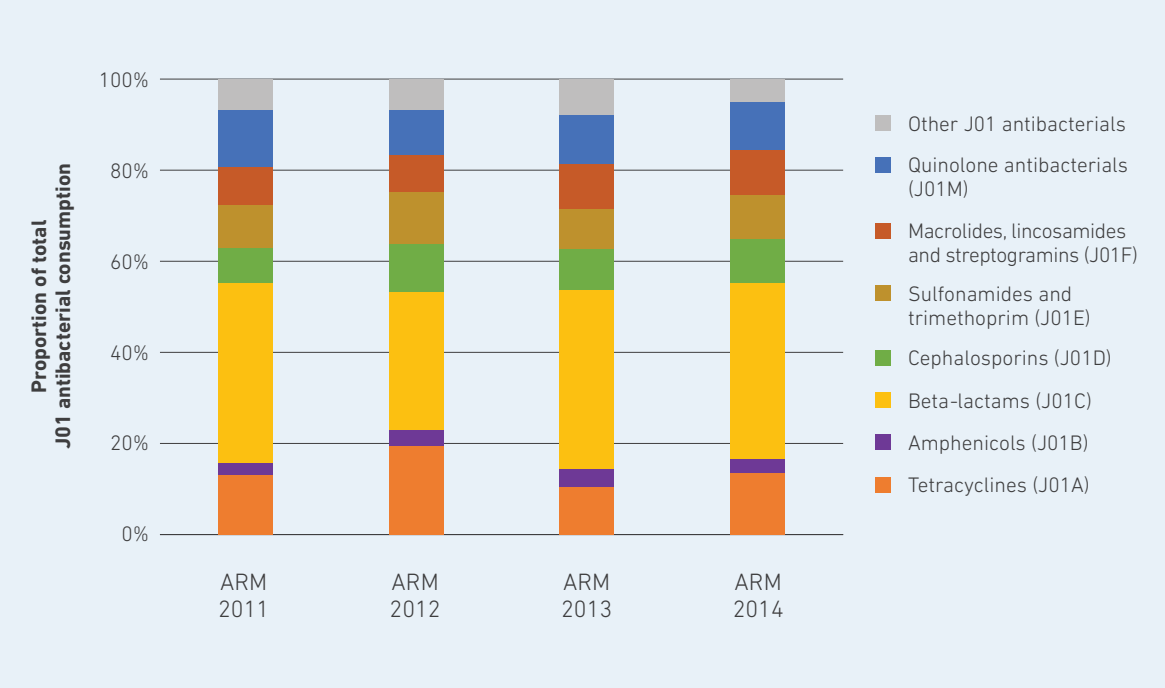

Fig. 5.3 Relative consumption of J01 antibacterials by pharmacological subgroup

The relative use of the pharmacological subgroups remained reasonably stable over time, with some evidence of increased consumption of cephalosporins (J01D), at 7.6% in 2011 and 9.5% in 2014, and macrolides, lincosamides and streptogramins (J01F), at 8.3% in 2011 and 9.9% in 2014 (Table 5.4).

Table 5.4 Relative consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	Consumption as proportion of total J01 consumption (%)[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	13.1	19.5	10.5	13.5
Amphenicols (J01B)	2.4	3.4	3.8	2.9
Beta-lactams (J01C)	39.7	30.3	39.3	38.8
Cephalosporins (J01D)	7.6	10.4	8.9	9.5
Sulfonamides and trimethoprim (J01E)	9.5	11.5	8.7	9.7
Macrolides, lincosamides and streptogramins (J01F)	8.3	8.2	10.0	9.9
Quinolone antibacterials (J01M)	12.7	9.8	10.6	10.6
Other J01 antibacterials (J01G, J01R, J01X)	6.7	6.8	8.0	5.0

[a] Total percentages may vary slightly owing to rounding.

5.3.2 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

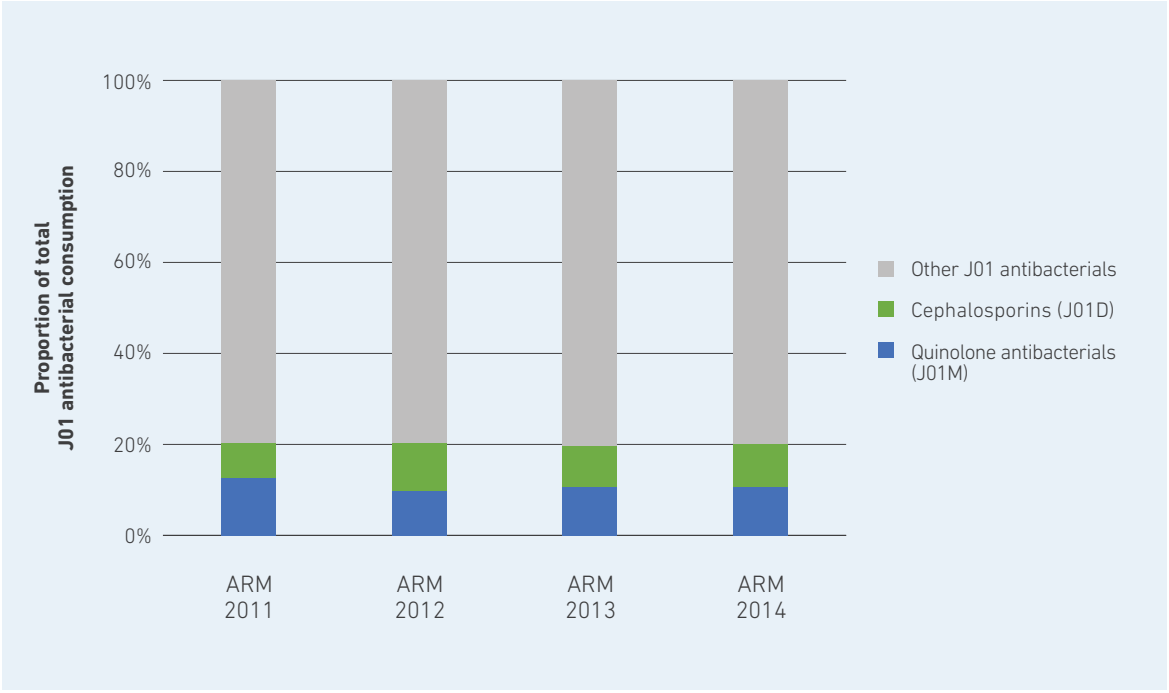

Fig. 5.4 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Cephalosporins and quinolones are broad-spectrum antibiotics and are considered second-line antibiotics in most prescribing guidelines. Generally, it is recommended that their use should be restricted to ensure availability as second-line therapy, should first-line antibiotics fail.

The relative consumption of cephalosporins and quinolones measured as a proportion of total J01 antibacterials is shown in Fig. 5.4 and summarized in Table 5.5.

There were small relative increases in consumption of cephalosporins, while consumption of quinolone antibacterials was stable. Together these two categories constituted 21% of J01 antibacterial consumption in 2014 (Table 5.5).

Table 5.5 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Class of antibacterial agents	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Quinolone antibacterials (J01M)	2 (13)	1.1 (10)	1.5 (11)	1.5 (11)
Cephalosporins (J01D)	1.2 (8)	1.2 (10)	1.2 (9)	1.4 (10)
Other J01 antibacterials	12.7 (80)	9.1 (80)	11.2 (80)	11.5 (80)
Total	**15.9**	**11.4**	**13.9**	**14.4**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

5.4 Relative consumption by choice of agent

5.4.1 Relative consumption of cephalosporins by generation

Third- and fourth-generation cephalosporins have a broader spectrum of activity than first- and second-generation agents, with enhanced coverage of both Gram-positive and Gram-negative organisms. WHO (2012) has identified third- and fourth-generation cephalosporins as some of the agents of highest priority for risk management to ensure that critically important antimicrobials are used prudently both in human and veterinary medicine.

The relative consumption of first-, second-, third- and fourth-generation cephalosporins in 2011–2014 is shown in Fig. 5.5 and summarized in Table 5.6.

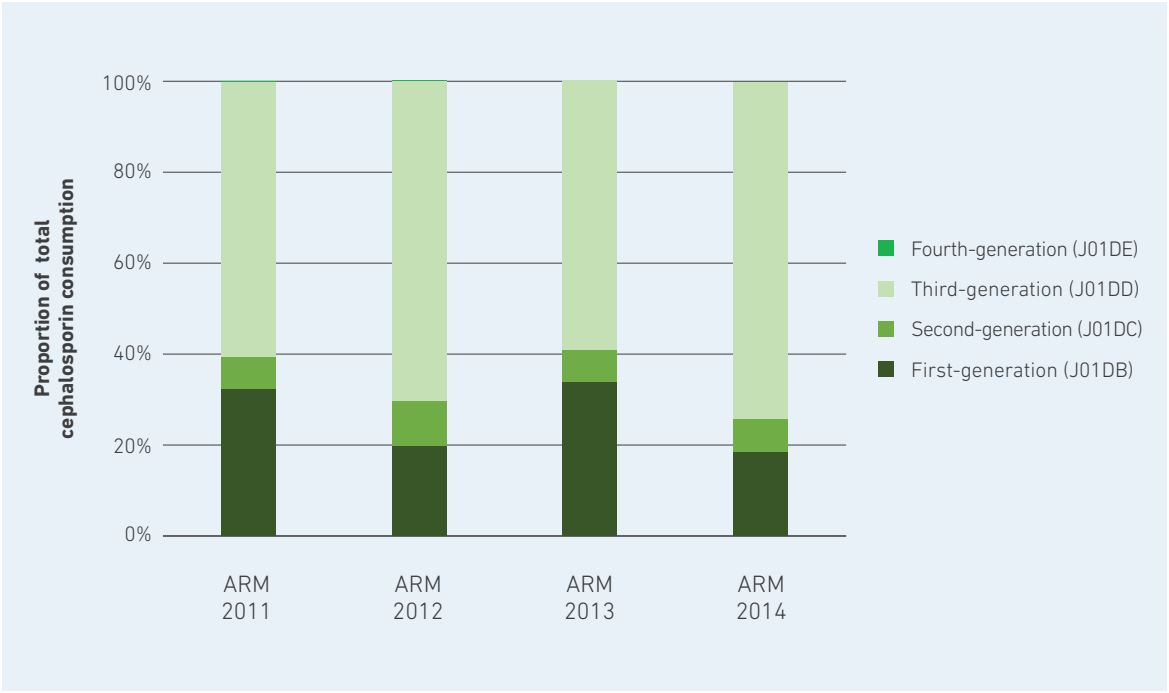

Fig. 5.5 Relative consumption of cephalosporins by generation

Consumption of both second- and fourth-generation cephalosporins over time was very limited. Most consumption was of third-generation agents (increasing from 60% in 2011 to 73% in 2014), matched by reductions in consumption of first- and second-generation cephalosporins combined (39% in 2011 to 27% in 2014; Table 5.6).

Table 5.6 Relative consumption of cephalosporins by generation

Generation	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
First- and second-generation (J01DB, J01DC)	0.5 (39)	0.4 (30)	0.5 (41)	0.4 (27)
Third-generation (J01DD)	0.7 (60)	0.8 (70)	0.7 (59)	1 (73)
Fourth-generation (J01DE)	<0.1	<0.1	<0.1	<0.1
Total	**1.2**	**1.2**	**1.2**	**1.4**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

5.4.1.1 Choice of first-generation cephalosporins (J01DB)

Table 5.7 summarizes the pattern of consumption of first-generation cephalosporins in 2011–2014. Cefalexin and cefazolin were the agents most consumed.

Table 5.7 Relative consumption of agents within first-generation cephalosporins (J01DB)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefalexin	0.1 (28)	<0.1	0.1 (24)	0.1 (47)
Cefalotin	<0.1	<0.1	<0.1	<0.1
Cefazolin	0.3 (72)	0.1 (62)	0.3 (76)	0.1 (53)
Cefadroxil	<0.1	<0.1	<0.1	<0.1
Cefradine	<0.1	<0.1	<0.1	<0.1
Total	**0.4**	**0.2**	**0.4**	**0.2**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

5.4.1.2 Choice of second-generation cephalosporins (J01DC)

Cefuroxime was the most consumed of the second-generation agents, with very low levels of consumption across the category.

5.4.1.3 Choice of third-generation cephalosporins (J01DD)

Table 5.8 summarizes the pattern of consumption of third-generation cephalosporins in 2011–2014. Consumption was dominated by ceftriaxone.

Table 5.8 Relative consumption of agents within third-generation cephalosporins (J01DD)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefotaxime	<0.1	<0.1	<0.1	<0.1
Ceftazidime	<0.1	<0.1	<0.1	<0.1
Ceftriaxone	0.7 (91)	0.7 (90)	0.6 (87)	0.9 (91)
Cefixime	<0.1	<0.1	<0.1	<0.1
Cefodizime	<0.1	<0.1	<0.1	<0.1
Cefoperazone	<0.1	<0.1	<0.1	<0.1
Cefpodoxime	<0.1	<0.1	<0.1	<0.1
Ceftibuten	<0.1	<0.1	<0.1	<0.1
Cefdinir	<0.1	<0.1	<0.1	<0.1
Cefoperazone, combinations	–	–	<0.1	<0.1
Total	**0.7**	**0.8**	**0.7**	**1.0**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

5.4.1.4 Choice of fourth-generation cephalosporins (J01DE)

Consumption of any of the fourth-generation cephalosporins was very limited.

5.4.2 Relative consumption of agents within fluoroquinolones (J01MA)

Quinolone antibacterials comprised around 11% of consumption of J01 antibacterials during 2011–2014 (see Table 5.4). Almost all quinolone consumption was from the fluoroquinolone category (J01MA). The most consumed agent was ciprofloxacin, with lower consumption of ofloxacin and moxifloxacin (Table 5.9).

Table 5.9 Relative consumption of agents within fluoroquinolones (J01MA)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Ofloxacin	0.1 (6)	0.2 (20)	0.1 (8)	0.2 (11)
Ciprofloxacin	1.1 (58)	0.5 (52)	1 (72)	1 (71)
Pefloxacin	<0.1	<0.1	<0.1	<0.1
Norfloxacin	0.1 (6)	0.1 (10)	0.1 (8)	<0.1
Lomefloxacin	<0.1	<0.1	<0.1	<0.1
Fleroxacin	<0.1	<0.1	<0.1	<0.1
Rufloxacin	<0.1	<0.1	<0.1	<0.1
Levofloxacin	0.5 (25)	<0.1	<0.1	<0.1
Moxifloxacin	<0.1	0.1 (10)	<0.1	0.1 (10)
Gemifloxacin	<0.1	<0.1	<0.1	<0.1
Gatifloxacin	<0.1	<0.1	<0.1	<0.1
Total	**1.9**	**1.0**	**1.4**	**1.4**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

5.4.3 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

The addition of clavulanic acid to amoxicillin extends the spectrum of activity of amoxicillin against beta-lactamase-producing bacteria. Amoxicillin and clavulanic acid is recommended as second-line treatment in many treatment guidelines.

Table 5.10 summarizes the relative consumption of amoxicillin and broader-spectrum amoxicillin and clavulanic acid. Amoxicillin was the more consumed agent in all years reported, although there is evidence of increasing consumption of amoxicillin and clavulanic acid (20% in 2011, 33% in 2014).

Table 5.10 Relative consumption of amoxicillin and amoxicillin and clavulanic acid

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Amoxicillin (J01CA04)	4.3 (80)	1.9 (64)	3.8 (76)	3.5 (67)
Amoxicillin and clavulanic acid (J01CR02)	1 (20)	1.1 (36)	1.2 (24)	1.7 (33)
Total	**5.3**	**3.1**	**5.0**	**5.2**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

5.5 The 10 most consumed agents

While the number of J01 antibacterial agents available is large, there is considerable evidence from ESAC-Net and other analyses that consumption tends to be concentrated in a relatively small number.

5.5.1 The 10 most consumed agents – oral formulation

Table 5.11 summarizes consumption of the oral agents that comprise the 10 most consumed in 2014. Six agents (amoxicillin, amoxicillin and enzyme inhibitor, doxycycline, sulfamethoxazole and trimethoprim, ciprofloxacin and azithromycin) account for almost 77% of consumption.

Table 5.11 The 10 most consumed agents – oral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Amoxicillin	3.52	3.52	3.52	3.52	3.52	3.52	3.52	3.52	3.52	3.52
Amoxicillin and enzyme inhibitor	1.69	1.69	1.69	1.69	1.69	1.69	1.69	1.69	1.69	
Doxycycline	1.64	1.64	1.64	1.64	1.64	1.64	1.64	1.64		
Sulfamethoxazole and trimethoprim	1.36	1.36	1.36	1.36	1.36	1.36	1.36			
Ciprofloxacin	0.95	0.95	0.95	0.95	0.95	0.95				
Azithromycin	0.74	0.74	0.74	0.74	0.74					
Clarithromycin	0.49	0.49	0.49	0.49						
Nitrofurantoin	0.49	0.49	0.49							
Chloramphenicol	0.42	0.42								
Tetracycline	0.32									
Total consumption for this group of agents	**11.62**	**11.30**	**10.89**	**10.40**	**9.90**	**9.16**	**8.20**	**6.84**	**5.21**	**3.52**
Total consumption for all oral J01 antibacterials	**12.93**	**12.93**	**12.93**	**12.93**	**12.93**	**12.93**	**12.93**	**12.93**	**12.93**	**12.93**
Proportion (%) of total consumption for oral J01 antibacterials	**89.8%**	**87.4%**	**84.2%**	**80.4%**	**76.5%**	**70.8%**	**63.4%**	**52.9%**	**40.2%**	**27.2%**

[a] DDD: daily defined dose.

5.5.2 The 10 most consumed agents – parenteral formulation

Table 5.12 summarizes consumption of the 10 most consumed parenteral agents in 2014. Three of these (ceftriaxone, cefazolin and benzylpenicillin) account for 75% of consumption.

Table 5.12 The 10 most consumed agents – parenteral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Ceftriaxone	0.92	0.92	0.92	0.92	0.92	0.92	0.92	0.92	0.92	0.92
Cefazolin	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	
Benzylpenicillin	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08		
Streptomycin	0.08	0.08	0.08	0.08	0.08	0.08	0.08			
Ampicillin	0.04	0.04	0.04	0.04	0.04	0.04				
Ciprofloxacin	0.04	0.04	0.04	0.04	0.04					
Metronidazole	0.03	0.03	0.03	0.03						
Moxifloxacin	0.03	0.03	0.03							
Cefotaxime	0.03	0.03								
Cefuroxime	0.03									
Total consumption for this group of agents	**1.42**	**1.39**	**1.36**	**1.33**	**1.29**	**1.26**	**1.22**	**1.14**	**1.05**	**0.92**
Total consumption for all parental J01 antibacterials	**1.51**	**1.51**	**1.51**	**1.51**	**1.51**	**1.51**	**1.51**	**1.51**	**1.51**	**1.51**
Proportion (%) of total consumption for parental J01 antibacterials	**93.8%**	**92.0%**	**90.2%**	**87.9%**	**85.6%**	**83.1%**	**80.4%**	**75.1%**	**69.6%**	**60.8%**

[a] DDD: daily defined dose.

5.6 Comments

Interpretation of the data presented in this chapter relies on an understanding of the national context. The analyses are based on import records and local manufacturer information, and the results suggest that import cycles may have an impact on the estimates and explain (in part) the fluctuations between years.

Consideration could be given to exploring the use of additional data sources, such as wholesaler data, to create more robust consumption estimates, including disaggregation to community and hospital sectors. A more detailed understanding of the patterns of antimicrobial consumption would identify areas for further investigation and allow development of targeted interventions to address potential problems identified in the consumption of antibacterials.

6. AZERBAIJAN

6.1 Data sources and years of data collection

Azerbaijan provided data for each of the four years of data collection (2011–2014). The main sources were import records provided by the drug agency (Table 6.1).

Table 6.1 Sources of data used for consumption estimates (2011–2014)

Year	Health care sector coverage	Data type	Data source (consumption)	Population	Data source (population)
2011	Total care	Import records	Drug agency	9 173 082	World Bank
2012	Total care	Import records	Drug agency	9 295 784	World Bank
2013	Total care	Import records	Drug agency	9 416 801	World Bank
2014	Total care	Import records	Drug agency	9 535 079	World Bank

6.2 Estimates of volumes of consumption of antibacterials for systemic use (J01)

Total consumption of antibacterials for systemic use (ATC class J01) is examined by route of administration (oral and parenteral formulations) and by pharmacological subgroup.

6.2.1 Total consumption of J01 antibacterials by route of administration

The consumption of oral and parenteral (injectable) formulations of J01 antibacterials is shown in Fig. 6.1 and summarized in Table 6.2 as DDD/1000 inhabitants per day (DID).

The data indicate some considerable fluctuations in total consumption of J01 antibacterials over time (17.1 DID in 2011 to 8.5 DID in 2014), with the highest estimate in 2012. Further investigation of the data sources used and completeness of data collection are needed to better understand

the results of the analyses shown here. Most notable is the high relative use of parenteral antibacterials – reported as 69% of total J01 consumption in 2014 (Table 6.2).

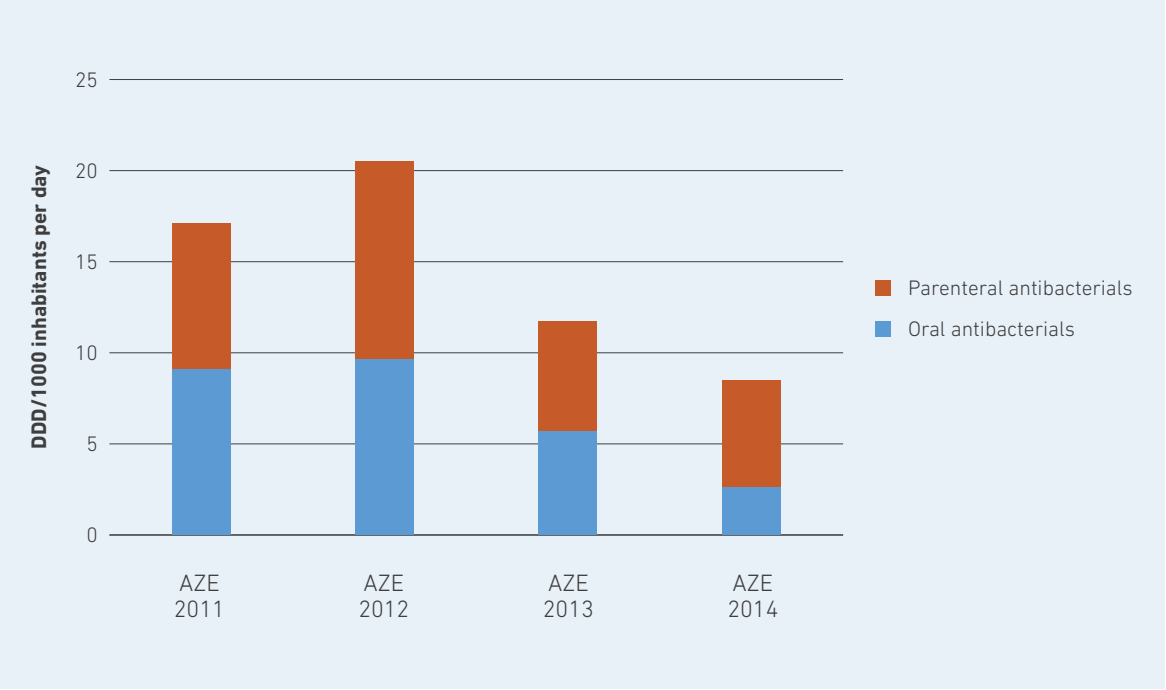

Fig. 6.1 Total consumption of J01 antibacterials by route of administration

DDD: defined daily dose.

Table 6.2 Total consumption of J01 antibacterials by route of administration

Route of administration	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Oral J01	9.1 (53)	9.6 (47)	5.7 (48)	2.6 (31)
Parenteral J01	8 (47)	10.9 (53)	6.1 (52)	5.8 (69)
Total	**17.1**	**20.5**	**11.7**	**8.5**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

6.2.2 Total consumption of J01 antibacterials by pharmacological subgroup

The consumption of J01 antibacterials by pharmacological subgroup is shown in Fig. 6.2 and summarized in Table 6.3.

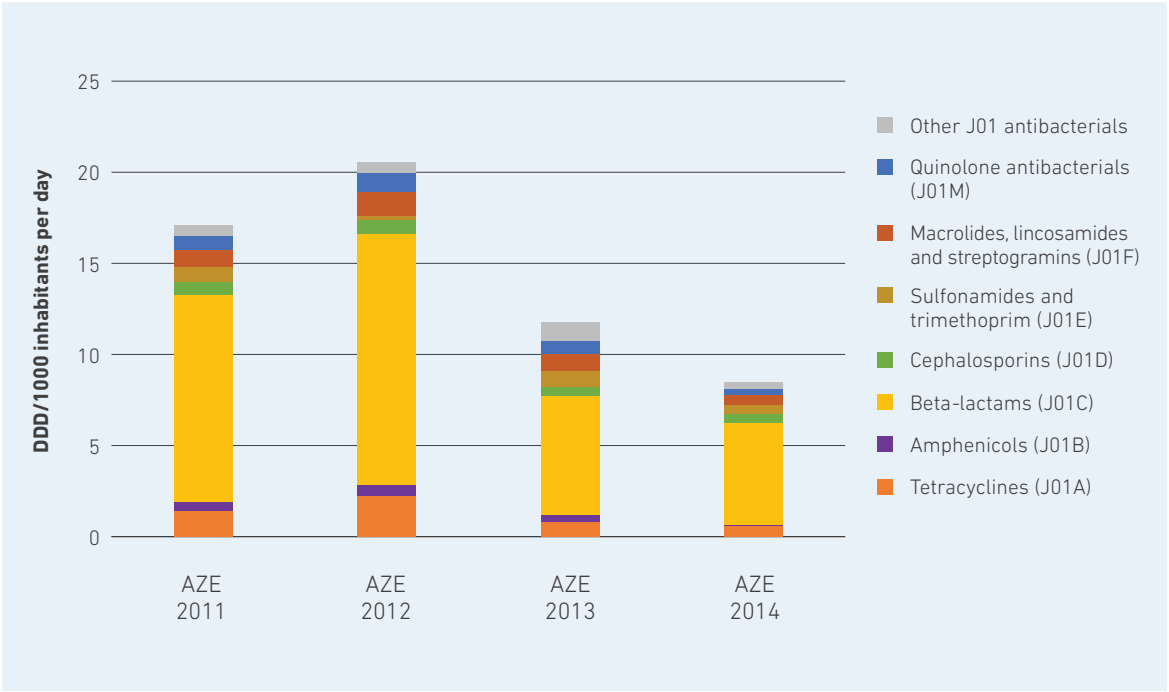

Fig. 6.2 Total consumption of J01 antibacterials by pharmacological subgroup

DDD: defined daily dose.

Table 6.3 Total consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	DDD/1000 inhabitants per day[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	1.4	2.2	0.8	0.6
Amphenicols (J01B)	0.5	0.6	0.3	0.1
Beta-lactams (J01C)	11.3	13.8	6.6	5.6
Cephalosporins (J01D)	0.8	0.7	0.5	0.5
Sulfonamides and trimethoprim (J01E)	0.8	0.3	0.9	0.5
Macrolides, lincosamides and streptogramins (J01F)	1.0	1.3	0.9	0.6
Quinolone antibacterials (J01M)	0.8	1.0	0.7	0.4
Other J01 antibacterials (J01G, J01R, J01X)	0.6	0.6	1.0	0.3
Total[b]	**17.1**	**20.5**	**11.7**	**8.5**

[a] DDD: daily defined dose. [b] Total amounts may vary slightly owing to rounding.

Given the uncertainty surrounding the reliability of the data for 2013 and 2014, it is difficult to comment on any patterns of change in absolute volumes of consumption for pharmacological subgroups.

6.3 Relative consumption of J01 antibacterials by subgroup

6.3.1 Relative consumption of J01 antibacterials by pharmacological subgroup

The relative consumption of pharmacological subgroups measured as a proportion of total J01 antibacterials is shown in Fig. 6.3 and summarized in Table 6.4.

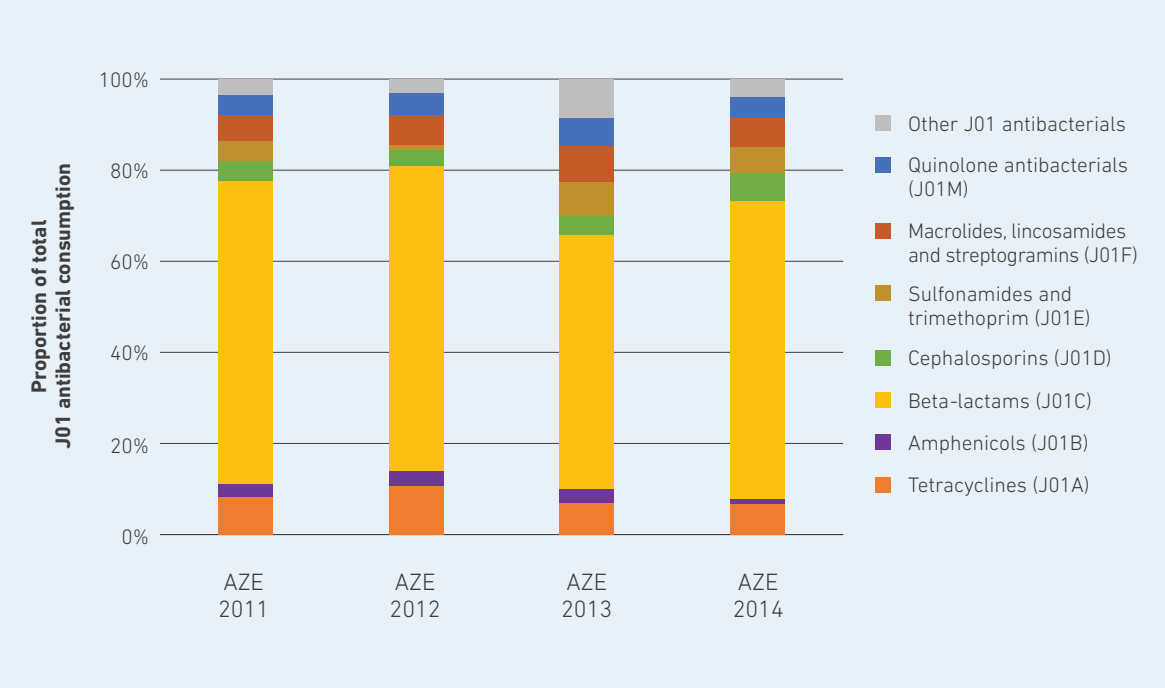

Fig. 6.3 Relative consumption of J01 antibacterials by pharmacological subgroup

The data illustrate the decline in relative consumption of tetracylines (J01A) and amphenicols (J01B) over time. Consumption of sulfonamides and trimethoprim (J01E) and macrolides, lincosamides and streptogramins (J01F) increased over time. Beta-lactams (J01C) was the most consumed pharmacological subgroup (65.6% of total J01 consumption in 2014) (Table 6.4).

Table 6.4 Relative consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	Consumption as proportion of total J01 consumption (%)[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	8.2	10.7	6.9	6.7
Amphenicols (J01B)	2.9	3.1	2.9	0.9
Beta-lactams (J01C)	66.3	67.0	55.8	65.6
Cephalosporins (J01D)	4.4	3.5	4.4	6.1
Sulfonamides and trimethoprim (J01E)	4.6	1.3	7.4	5.6
Macrolides, lincosamides and streptogramins (J01F)	5.6	6.5	7.9	6.5
Quinolone antibacterials (J01M)	4.4	4.8	6.2	4.5
Other J01 antibacterials (J01G, J01R, J01X)	3.5	3.1	8.5	4.1

[a] Total percentages may vary slightly owing to rounding.

6.3.2 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Cephalosporins and quinolones are broad-spectrum antibiotics and are considered second-line antibiotics in most prescribing guidelines. Generally, it is recommended that their use should be restricted to ensure availability as second-line therapy, should first-line antibiotics fail.

The relative consumption of cephalosporins and quinolones measured as a proportion of total J01 antibacterials is shown in Fig. 6.4 and summarized in Table 6.5.

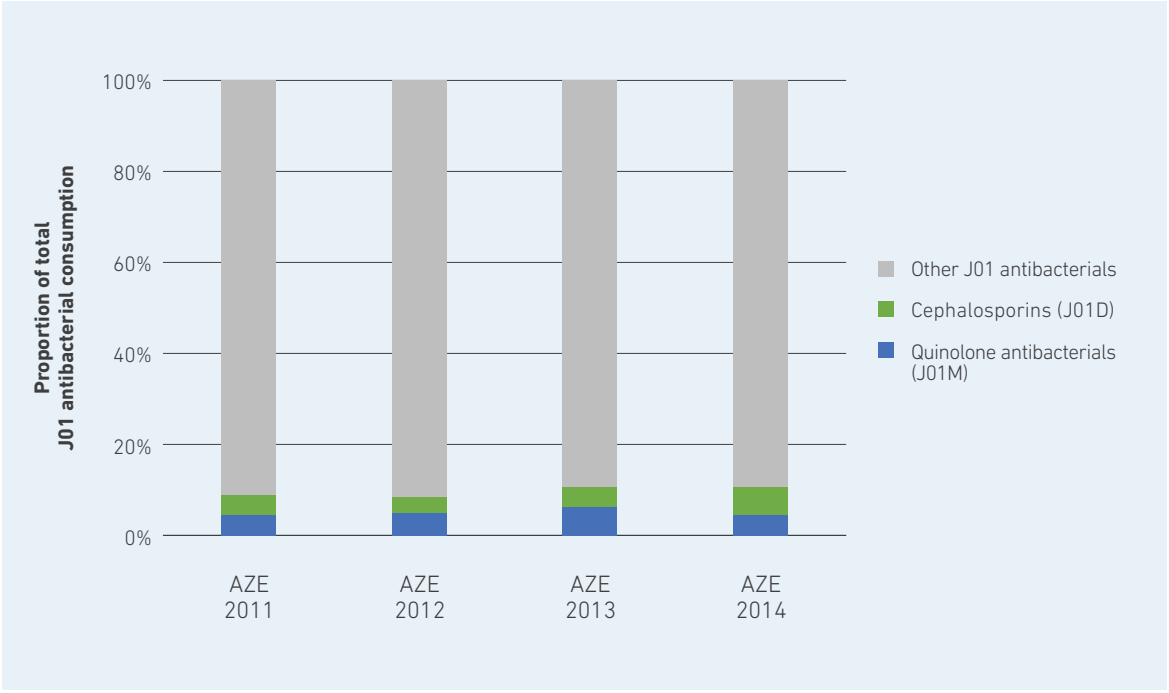

Fig. 6.4 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

The consumption of cephalosporins and quinolone antibacterials was relatively stable over time. Together these two categories constitute around 10% of J01 antibacterial consumption in 2014 (Table 6.5).

Table 6.5 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Class of antibacterial agents	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Quinolone antibacterials (J01M)	0.8 (4)	1 (5)	0.7 (6)	0.4 (4)
Cephalosporins (J01D)	0.8 (4)	0.7 (4)	0.5 (4)	0.5 (6)
Other J01 antibacterials	15.6 (91)	18.8 (92)	10.5 (89)	7.6 (89)
Total	**17.1**	**20.5**	**11.7**	**8.5**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

6.4 Relative consumption by choice of agent

6.4.1 Relative consumption of cephalosporins by generation

Third- and fourth-generation cephalosporins have a broader spectrum of activity than first- and second-generation agents, with enhanced coverage of both Gram-positive and Gram-negative

organisms. WHO (2012) has identified third- and fourth-generation cephalosporins as some of the agents of highest priority for risk management to ensure that critically important antimicrobials are used prudently both in human and veterinary medicine.

The relative consumption of first-, second-, third- and fourth-generation cephalosporins in 2011–2014 is shown in Fig. 6.5 and summarized in Table 6.6.

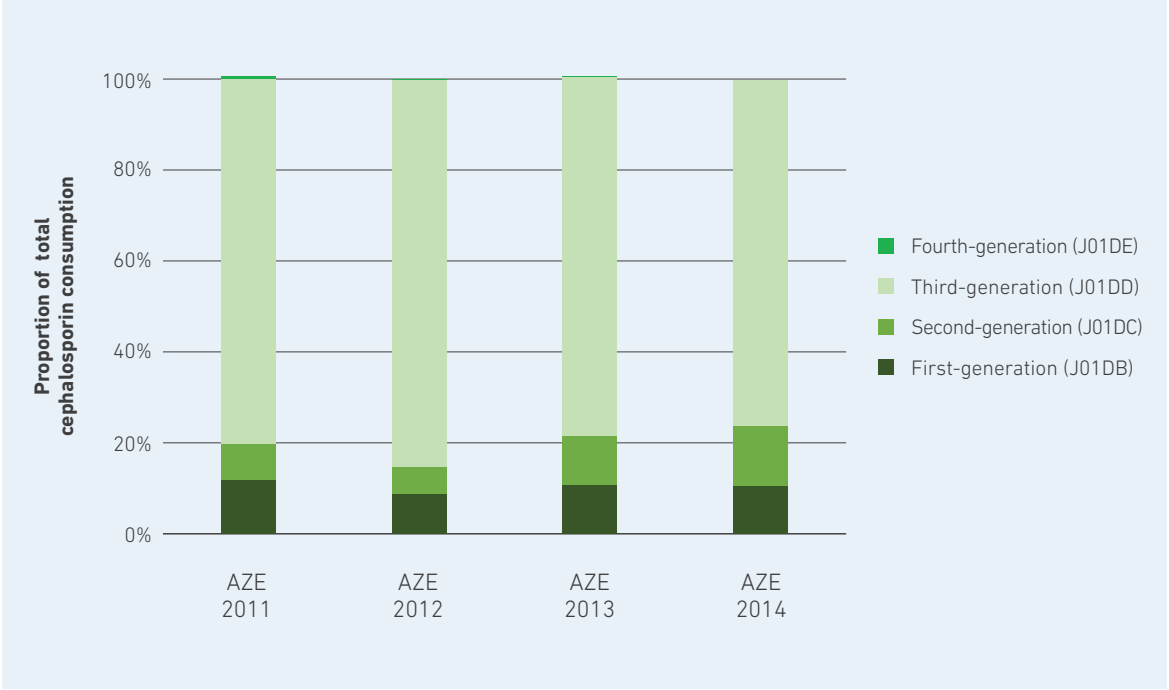

Fig. 6.5 Relative consumption of cephalosporins by generation

There was very low consumption of fourth-generation cephalosporins reported, with consumption of first- and second-generation agents combined around 24% of total cephalosporin consumption. Third-generation cephalosporins were most consumed (Table 6.6).

Table 6.6 Relative consumption of cephalosporins by generation

Generation	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
First- and second-generation (J01DB-C)	0.1 (20)	0.1 (15)	0.1 (21)	0.1 (24)
Third-generation (J01DD)	0.6 (80)	0.6 (85)	0.4 (78)	0.4 (76)
Fourth-generation (J01DE)	<0.1	<0.1	<0.1	<0.1
Total	**0.8**	**0.7**	**0.5**	**0.5**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

6.4.1.1 Choice of first-generation cephalosporins (J01DB)

Together, first- and second-generation agents contributed 0.1 DID to total J01 consumption in 2011–2014. Levels of consumption of first-generation cephalosporins (cefalexin, cefazolin and cefadroxil) were low.

6.4.1.2 Choice of second-generation cephalosporins (J01DC)

Levels of consumption of second-generation cephalosporins (cefuroxime, cefaclor) were low in 2011–2014.

6.4.1.3 Choice of third-generation cephalosporins (J01DD)

Table 6.7 summarizes the pattern of consumption of third-generation cephalosporins in 2011–2014. Ceftriaxone was the most consumed agent.

Table 6.7 Relative consumption of agents within third-generation cephalosporins (J01DD)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefotaxime	<0.1	0.1 (19)	<0.1	<0.1
Ceftazidime	<0.1	<0.1	<0.1	<0.1
Ceftriaxone	0.5 (81)	0.5 (77)	0.3 (83)	0.3 (83)
Cefixime	<0.1	<0.1	<0.1	<0.1
Cefoperazone	<0.1	<0.1	<0.1	–
Total	**0.6**	**0.6**	**0.4**	**0.4**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

6.4.1.4 Choice of fourth-generation cephalosporins (J01DE)

Levels of consumption of the fourth-generation cephalosporins (cefepime and cefpirome) were low in 2011–2014.

6.4.2 Relative consumption of agents within fluoroquinolones (J01MA)

Quinolone antibacterials comprised around 4–6% of consumption of J01 antibacterials during 2011–2014 (see Table 6.4). Almost all consumption was from the fluoroquinolone category (J01MA). The most consumed agents were levofloxacin and ofloxacin (Table 6.8).

Table 6.8 Relative consumption of agents within fluoroquinolones (J01MA)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Ofloxacin	0.2 (25)	0.3 (27)	0.2 (29)	0.1 (35)
Ciprofloxacin	0.2 (31)	0.2 (23)	0.2 (23)	<0.1
Norfloxacin	<0.1	<0.1	<0.1	<0.1
Levofloxacin	0.3 (42)	0.4 (39)	0.2 (33)	0.1 (38)
Moxifloxacin	<0.1	0.1 (10)	0.1 (14)	<0.1
Gemifloxacin	–	–	–	<0.1
Total	**0.8**	**1.0**	**0.7**	**0.4**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

6.4.3 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

The addition of clavulanic acid to amoxicillin extends the spectrum of activity of amoxicillin against beta-lactamase-producing bacteria. Amoxicillin and clavulanic acid is recommended as second-line treatment in many treatment guidelines.

Table 6.9 summarizes the relative consumption of amoxicillin and broader-spectrum amoxicillin and clavulanic acid. Amoxicillin was the more consumed agent in all years reported.

Table 6.9 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Amoxicillin (J01CA04)	4 (93)	3.3 (94)	1.3 (84)	0.3 (57)
Amoxicillin and clavulanic acid (J01CR02)	0.3 (7)	0.2 (6)	0.2 (16)	0.2 (43)
Total	**4.4**	**3.5**	**1.5**	**0.5**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

Further investigation is required to understand the large relative increases in consumption of amoxicillin and clavulanic acid compared to amoxicillin over time (7% in 2011, 43% in 2014).

6.5 The 10 most consumed agents

While the number of J01 antibacterial agents available is large, there is considerable evidence from ESAC-Net and other analyses that consumption tends to be concentrated in a relatively small number.

6.5.1 The 10 most consumed agents – oral formulation

Table 6.10 summarizes consumption of the oral agents that comprise the 10 most consumed in 2014. Eight agents (doxycycline, azithromycin, sulfadimethoxine, amoxicillin, amoxicillin and enzyme inhibitor, sulfamethoxazole and trimethoprim, clarithromycin and tetracycline) account for almost 77% of consumption.

6.5.2 The 10 most consumed agents – parenteral formulation

Table 6.11 summarizes consumption of the 10 most consumed parenteral agents in 2014. One of these (ampicillin) accounts for almost 74% of consumption; two penicillins (ampicillin and benyzylpenicillin) account for almost 82% of consumption.

Table 6.10 The 10 most consumed agents – oral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Doxycycline	0.42	0.42	0.42	0.42	0.42	0.42	0.42	0.42	0.42	0.42
Azithromycin	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	
Sulfadimethoxine	0.29	0.29	0.29	0.29	0.29	0.29	0.29	0.29		
Amoxicillin	0.27	0.27	0.27	0.27	0.27	0.27	0.27			
Amoxicillin and enzyme inhibitor	0.20	0.20	0.20	0.20	0.20	0.20				
Sulfamethoxazole and trimethoprim	0.18	0.18	0.18	0.18	0.18					
Clarithromycin	0.17	0.17	0.17	0.17						
Tetracycline	0.15	0.15	0.15							
Levofloxacin	0.13	0.13								
Ofloxacin	0.12									
Total consumption for this group of agents	**2.26**	**2.14**	**2.02**	**1.86**	**1.70**	**1.51**	**1.31**	**1.04**	**0.75**	**0.42**
Total consumption for all oral J01 antibacterials	**2.63**	**2.63**	**2.63**	**2.63**	**2.63**	**2.63**	**2.63**	**2.63**	**2.63**	**2.63**
Proportion (%) of total consumption for oral J01 antibacterials	**85.9%**	**81.3%**	**76.5%**	**70.7%**	**64.4%**	**57.5%**	**49.8%**	**39.3%**	**28.3%**	**15.9%**

[a] DDD: daily defined dose.

Table 6.11 The 10 most consumed agents – parenteral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Ampicillin	4.30	4.30	4.30	4.30	4.30	4.30	4.30	4.30	4.30	4.30
Benzylpenicillin	0.46	0.46	0.46	0.46	0.46	0.46	0.46	0.46	0.46	
Ceftriaxone	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33		
Ampicillin and enzyme inhibitor	0.17	0.17	0.17	0.17	0.17	0.17	0.17			
Amikacin	0.11	0.11	0.11	0.11	0.11	0.11				
Combinations of penicillins	0.09	0.09	0.09	0.09	0.09					
Metronidazole	0.08	0.08	0.08	0.08						
Streptomycin	0.06	0.06	0.06							
Kanamycin	0.06	0.06								
Cefazolin	0.05									
Total consumption for this group of agents	**5.69**	**5.65**	**5.59**	**5.53**	**5.45**	**5.36**	**5.25**	**5.08**	**4.76**	**4.30**
Total consumption for all parental J01 antibacterials	**5.84**	**5.84**	**5.84**	**5.84**	**5.84**	**5.84**	**5.84**	**5.84**	**5.84**	**5.84**
Proportion (%) of total consumption for parental J01 antibacterials	**97.5%**	**96.7%**	**95.7%**	**94.7%**	**93.4%**	**91.8%**	**90.0%**	**87.1%**	**81.5%**	**73.6%**

[a] DDD: daily defined dose.

6.6 Comments

The analyses presented in this chapter provide annual consumption estimates. The data indicate some considerable fluctuations in total consumption of J01 antibacterials over time, and further investigation of the sources used and completeness of data collection are needed to better understand the results.

7. BELARUS

7.1 Data sources and years of data collection

Belarus data were available for each of the four years of data collection (2011–2014). The main sources were import records provided by the drug agency and information provided by local pharmaceutical manufacturers (Table 7.1). Further information on the estimates provided by local manufacturers was not available.

Table 7.1 Sources of data used for consumption estimates (2011–2014)

Year	Health care sector coverage	Data type	Data source (consumption)	Population	Data source (population)
2011	Total care	Import records Sales records	Drug agency Local manufacturers	9 473 000	World Bank
2012	Total care	Import records Sales records	Drug agency Local manufacturers	9 464 000	World Bank
2013	Total care	Import records Sales records	Drug agency Local manufacturers	9 466 000	World Bank
2014	Total care	Import records Sales records	Drug agency Local manufacturers	9 483 000	World Bank

7.2 Estimates of volumes of consumption of antibacterials for systemic use (J01)

Total consumption of antibacterials for systemic use (ATC class J01) is examined by route of administration (oral and parenteral formulations) and by pharmacological subgroup.

7.2.1 Total consumption of J01 antibacterials by route of administration

The consumption of oral and parenteral (injectable) formulations of J01 antibacterials is shown in Fig. 7.1 and summarized in Table 7.2 as DDD/1000 inhabitants per day (DID).

The data indicate some fluctuations in total consumption of J01 antibacterials over time (17.9 DID in 2011 to 20.0 DID in 2014), with the highest estimate in 2013; however, this might be explained in part by the import cycles for these medicines.

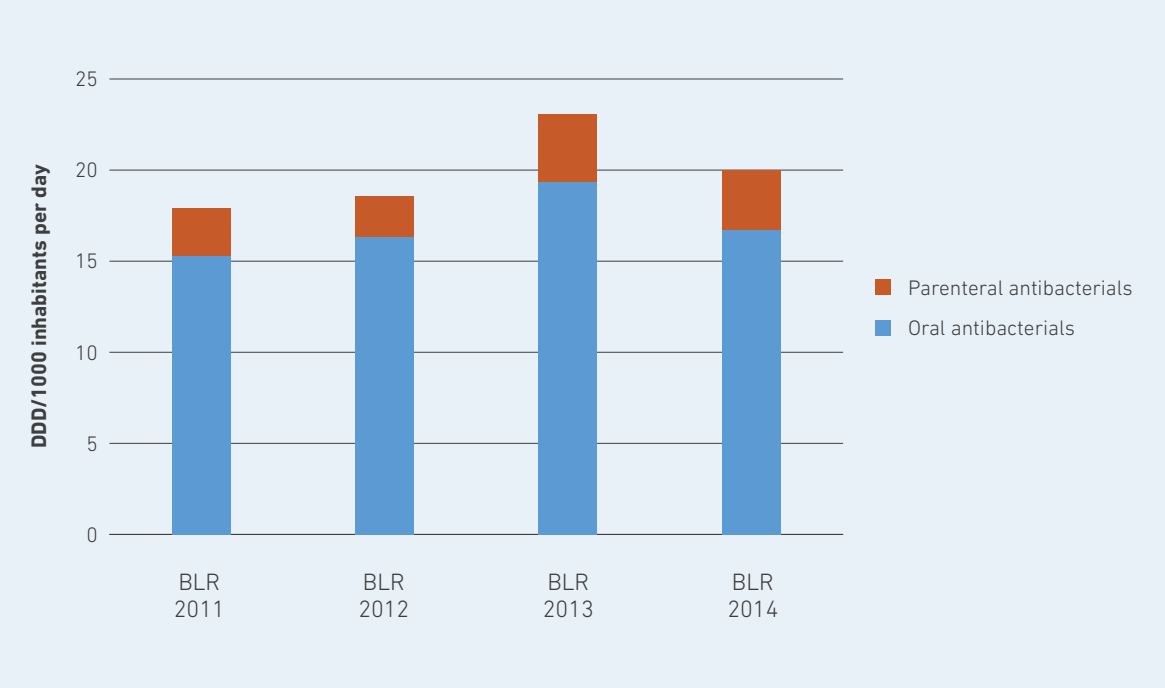

Fig. 7.1 Total consumption of J01 antibacterials by route of administration

DDD: defined daily dose.

The relative consumption of parenteral antibacterials remained reasonably stable at around 16% of total J01 consumption (Table 7.2).

Table 7.2 Total consumption of J01 antibacterials by route of administration

Route of administration	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Oral J01	15.3 (85)	16.3 (88)	19.3 (84)	16.7 (84)
Parenteral J01	2.6 (15)	2.2 (12)	3.7 (16)	3.3 (16)
Total	**17.9**	**18.6**	**23.1**	**20.0**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

7.2.2 Total consumption of J01 antibacterials by pharmacological subgroup

The consumption of J01 antibacterials by pharmacological subgroup is shown in Fig. 7.2 and summarized in Table 7.3.

Numerically, the largest changes in consumption of pharmacological subgroups occurred in macrolides, lincosamides and streptogramins (J01F), which increased from 1.6 DID in 2011 to 2.8 DID in 2014, with a peak of 3.1 DID in 2013. The highest levels of consumption were beta-lactams (J01C), at 6.7 DID in 2011 and 7.1 DID in 2014, and cephalosporins (J01D), at 2.3 DID in 2011 and 3.1 DID in 2014.

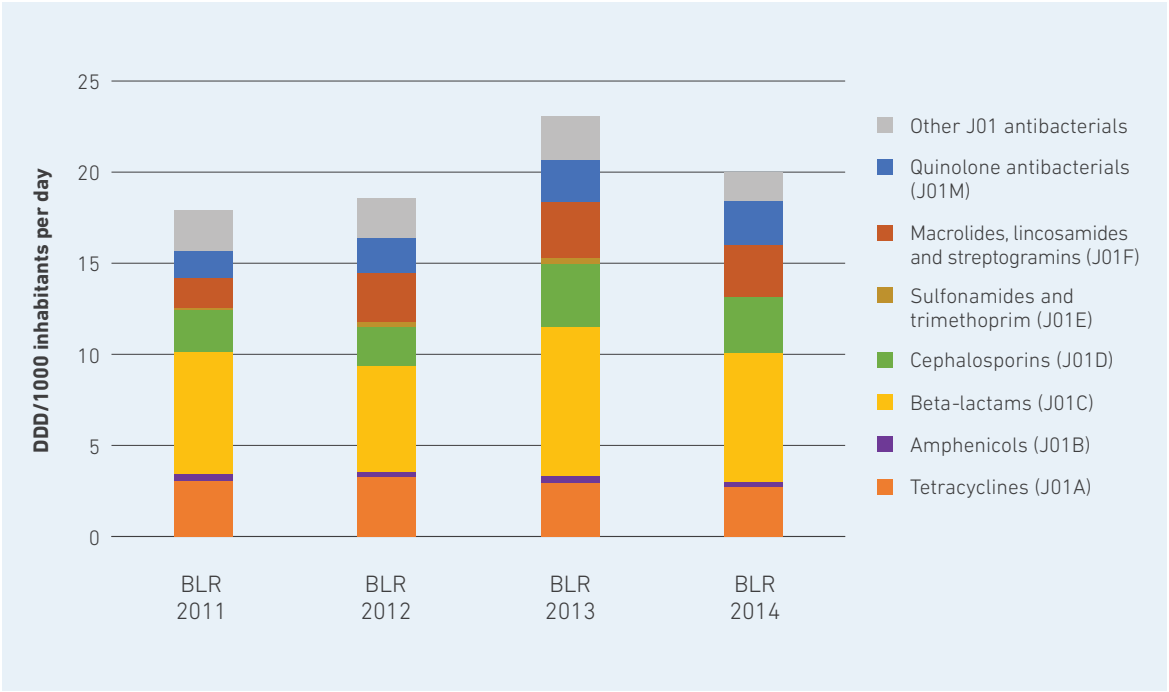

Fig. 7.2 Total consumption of J01 antibacterials by pharmacological subgroup

DDD: defined daily dose.

Table 7.3 Total consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	DDD/1000 inhabitants per day[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	3.0	3.3	2.9	2.7
Amphenicols (J01B)	0.4	0.2	0.3	0.2
Beta-lactams (J01C)	6.7	5.9	8.2	7.1
Cephalosporins (J01D)	2.3	2.1	3.5	3.1
Sulfonamides and trimethoprim (J01E)	0.1	0.3	0.3	<0.1
Macrolides, lincosamides and streptogramins (J01F)	1.6	2.7	3.1	2.8
Quinolone antibacterials (J01M)	1.5	1.9	2.3	2.5
Other J01 antibacterials (J01G, J01X)	2.3	2.2	2.4	1.6
Total[b]	**17.9**	**18.6**	**23.1**	**20.0**

[a] DDD: daily defined dose. [b] Total amounts may vary slightly owing to rounding.

7.3 Relative consumption of J01 antibacterials by subgroup

7.3.1 Relative consumption of J01 antibacterials by pharmacological subgroup

The relative consumption of pharmacological subgroups measured as a proportion of total J01 antibacterials is shown in Fig. 7.3 and summarized in Table 7.4.

The data illustrate the decline in relative consumption of tetracylines (J01A) and amphenicols (J01B) over time. While it is a quantitatively a smaller decline, consumption of sulfonamides and trimethoprim (J01E) also decreased over time.

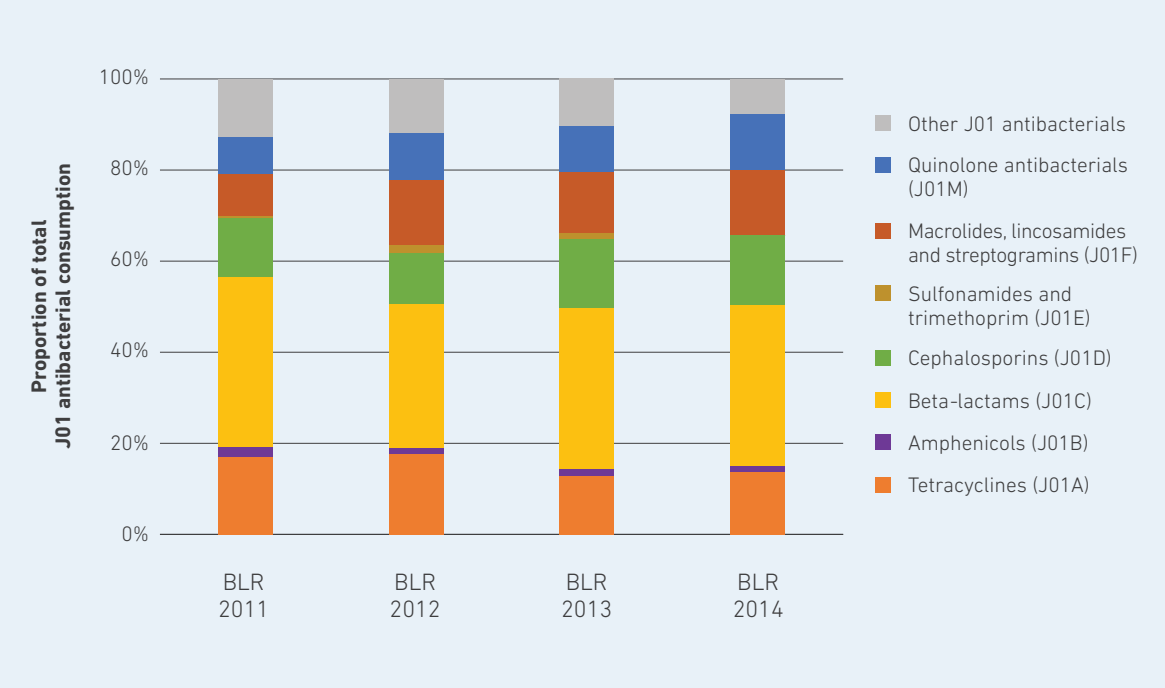

Fig. 7.3 Relative consumption of J01 antibacterials by pharmacological subgroup

Beta-lactams (J01C) was the most consumed pharmacological subgroup, at 35.4% of total J01 consumption in 2014, followed by cephalosporins (J01D), at 15.4%, macrolides, lincosamides and streptogramins (J01F), at 14.1%, and tetracyclines (J01A), at 13.7% (Table 7.4).

Table 7.4 Relative consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	Consumption as proportion of total J01 consumption (%)[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	16.9	17.7	12.8	13.7
Amphenicols (J01B)	2.3	1.2	1.5	1.2
Beta-lactams (J01C)	37.2	31.6	35.5	35.4
Cephalosporins (J01D)	13.0	11.4	15.0	15.4
Sulfonamides and trimethoprim (J01E)	0.4	1.6	1.5	<0.1
Macrolides, lincosamides and streptogramins (J01F)	9.2	14.3	13.3	14.1
Quinolone antibacterials (J01M)	8.3	10.4	10.0	12.3
Other J01 antibacterials (J01G, J01R, J01X)	12.6	11.8	10.3	7.9

[a] Total percentages may vary slightly owing to rounding.

7.3.2 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Cephalosporins and quinolones are broad-spectrum antibiotics and are considered second-line antibiotics in most prescribing guidelines. Generally, it is recommended that their use should be restricted to ensure availability as second-line therapy, should first-line antibiotics fail.

The relative consumption of cephalosporins and quinolones measured as a proportion of total J01 antibacterials is shown in Fig. 7.4 and summarized in Table 7.5.

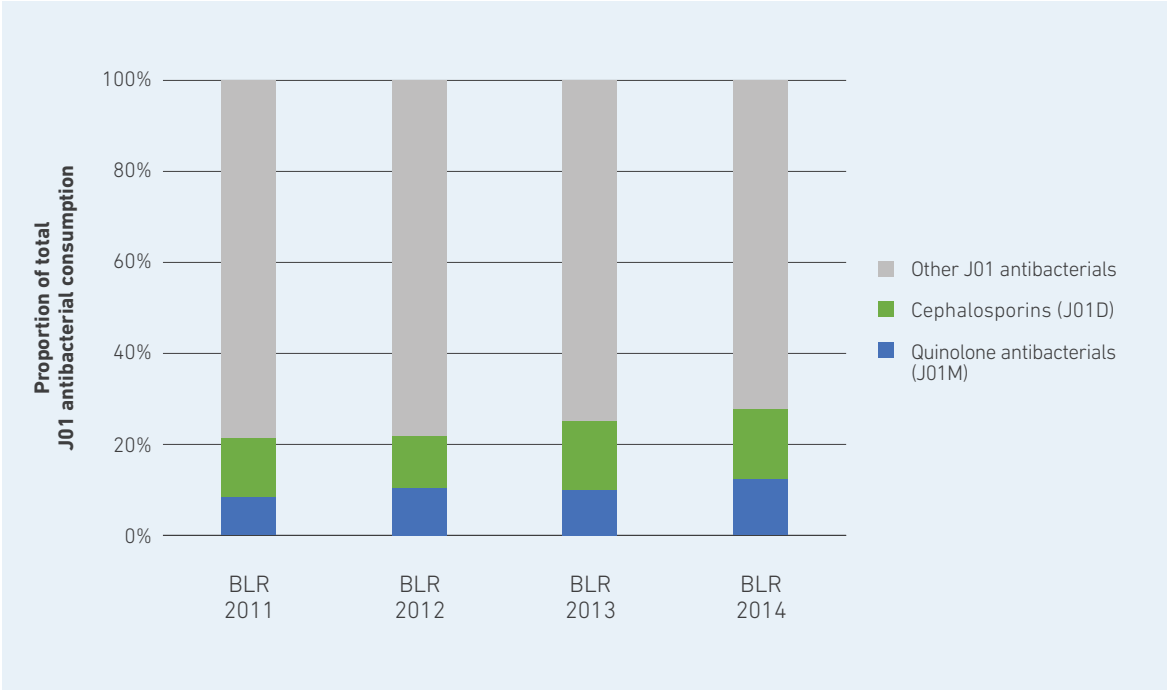

Fig. 7.4 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

There were small relative increases in consumption of both cephalosporins and quinolone antibacterials over time. Together these two categories constitute 27% of J01 antibacterial consumption in 2014 (Table 7.5).

Table 7.5 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Class of antibacterial agents	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Quinolone antibacterials (J01M)	1.5 (8)	1.9 (10)	2.3 (10)	2.5 (12)
Cephalosporins (J01D)	2.3 (13)	2.1 (11)	3.5 (15)	3.1 (15)
Other J01 antibacterials	14.1 (79)	14.5 (78)	17.3 (75)	14.4 (72)
Total	**17.9**	**18.6**	**23.1**	**20.0**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

7.4 Relative consumption by choice of agent

7.4.1 Relative consumption of cephalosporins by generation

Third- and fourth-generation cephalosporins have a broader spectrum of activity than first- and second-generation agents, with enhanced coverage of both Gram-positive and Gram-negative

organisms. WHO (2012) has identified third- and fourth-generation cephalosporins as some of the agents of highest priority for risk management to ensure that critically important antimicrobials are used prudently both in human and veterinary medicine.

The relative consumption of first-, second-, third- and fourth-generation cephalosporins in 2011–2014 is shown in Fig. 7.5 and summarized in Table 7.6.

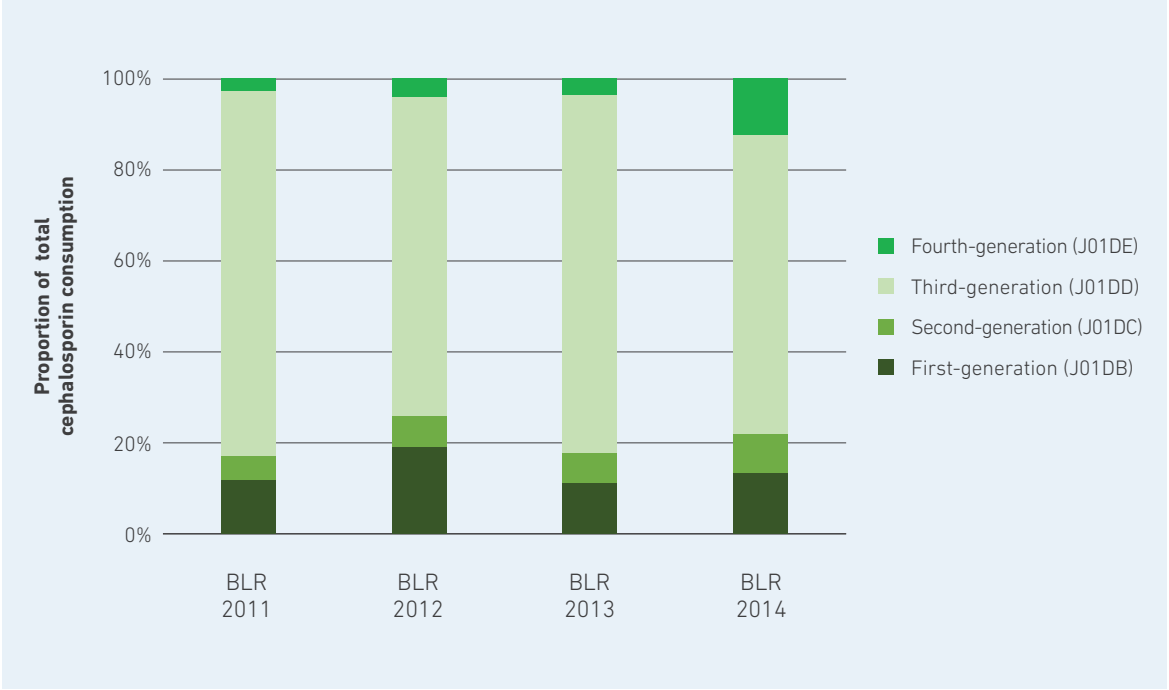

Fig. 7.5 Relative consumption of cephalosporins by generation

Increasing consumption of fourth-generation cephalosporins was reported over time (13% of reported cephalosporin consumption in 2014), with some suggestion of relative reductions in consumption of third-generation agents (decreasing from 80% in 2011 to 66% in 2014). Consumption of first- and second-generation agents was reasonably stable (Table 7.6).

Table 7.6 Relative consumption of cephalosporins by generation

Generation	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
First-generation (J01DB)	0.3 (12)	0.4 (19)	0.4 (11)	0.4 (13)
Second-generation (J01DC)	0.1 (5)	0.1 (7)	0.2 (6)	0.3 (9)
Third-generation (J01DD)	1.8 (80)	1.4 (70)	2.7 (79)	2 (66)
Fourth-generation (J01DE)	<0.1	<0.1	0.1 (4)	0.4 (13)
Total	**2.3**	**2.1**	**3.4**	**3.0**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

7.4.1.1 Choice of first-generation cephalosporins (J01DB)

Table 7.7 illustrates the pattern of consumption of first-generation cephalosporins in 2011–2014. Cefalexin and cefazolin were those most consumed.

Table 7.7 Relative consumption of agents within first-generation cephalosporins (J01DB)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefalexin	0.2 (62)	0.3 (82)	0.3 (85)	0.3 (64)
Cefazolin	0.1 (38)	<0.1	<0.1	0.1 (36)
Total	**0.3**	**0.4**	**0.4**	**0.4**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

7.4.1.2 Choice of second-generation cephalosporins (J01DC)

Table 7.8 summarizes the pattern of consumption of second-generation cephalosporins in 2011–2014. Cefuroxime was the most consumed agent.

Table 7.8 Relative consumption of agents within second-generation cephalosporins (J01DC)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefuroxime	<0.1	0.1 (79)	0.2 (98)	0.2 (96)
Cefaclor	<0.1	<0.1	<0.1	<0.1
Cefprozil	<0.1	<0.1	<0.1	<0.1
Total	**0.1**	**0.1**	**0.2**	**0.3**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

7.4.1.3 Choice of third-generation cephalosporins (J01DD)

Table 7.9 summarizes the pattern of consumption of third-generation cephalosporins in 2011–2014. Ceftriaxone and cefotaxime were those most consumed.

Table 7.9 Relative consumption of agents within third-generation cephalosporins (J01DD)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefotaxime	0.7 (35)	0.6 (40)	0.6 (22)	0.4 (22)
Ceftazidime	<0.1	<0.1	<0.1	<0.1
Ceftriaxone	1.2 (64)	0.8 (56)	2 (75)	1.5 (77)
Cefixime	<0.1	<0.1	<0.1	<0.1
Cefoperazone	<0.1	<0.1	<0.1	<0.1
Cefpodoxime	<0.1	<0.1	<0.1	<0.1
Ceftibuten	<0.1	<0.1	<0.1	<0.1
Cefdinir	<0.1	<0.1	<0.1	<0.1
Total	**1.8**	**1.4**	**2.7**	**2.0**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

7.4.1.4 Choice of fourth-generation cephalosporins (J01DE)

Table 7.10 summarizes the pattern of consumption of fourth-generation cephalosporins in 2011–2014. Cefpirome was the only agent consumed.

Table 7.10 Relative consumption of agents within fourth-generation cephalosporins (J01DE)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefpirome	<0.1	<0.1	0.1 (100)	0.4 (100)
Total	**<0.1**	**<0.1**	**0.1**	**0.4**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

7.4.2 Relative consumption of agents within fluoroquinolones (J01MA)

Quinolone antibacterials comprised around 10–12% of consumption of J01 antibacterials during 2011–2014 (see Table 7.4). Almost all of this consumption was from the fluoroquinolone category (J01MA). The most consumed fluoroquinolone agents were ciprofloxacin, levofloxacin and ofloxacin (Table 7.11).

Table 7.11 Relative consumption of agents within fluoroquinolones (J01MA)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Ofloxacin	0.4 (27)	0.4 (23)	0.3 (14)	0.3 (10)
Ciprofloxacin	0.5 (37)	0.7 (36)	0.8 (35)	1.4 (59)
Pefloxacin	<0.1	<0.1	<0.1	<0.1
Norfloxacin	0.2 (17)	0.3 (17)	0.3 (11)	0.2 (8)
Levofloxacin	0.2 (17)	0.4 (22)	0.8 (37)	0.5 (20)
Moxifloxacin	<0.1	<0.1	<0.1	<0.1
Gemifloxacin	<0.1	<0.1	<0.1	<0.1
Gatifloxacin	<0.1	<0.1	<0.1	<0.1
Total	**1.5**	**1.9**	**2.3**	**2.4**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

7.4.3 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

The addition of clavulanic acid to amoxicillin extends the spectrum of activity of amoxicillin against beta-lactamase-producing bacteria. Amoxicillin and clavulanic acid is recommended as second-line treatment in many treatment guidelines.

Table 7.12 summarizes the relative consumption of amoxicillin and broader-spectrum amoxicillin and clavulanic acid. Amoxicillin was the more consumed agent in all years reported.

Table 7.12 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Amoxicillin (J01CA04)	2.4 (53)	4.2 (79)	5.4 (71)	4.2 (64)
Amoxicillin and clavulanic acid (J01CR02)	2.1 (47)	1.1 (21)	2.2 (29)	2.4 (36)
Total	**4.5**	**5.3**	**7.6**	**6.6**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

7.5 The 10 most consumed agents

While the number of J01 antibacterial agents available is large, there is considerable evidence from ESAC-Net and other analyses that consumption tends to be concentrated in a relatively small number.

7.5.1 The 10 most consumed agents – oral formulation

Table 7.13 summarizes consumption of the oral agents that comprise the 10 most consumed in 2014. Six agents (amoxicillin, doxycycline, amoxicillin and enzyme inhibitor, azithromycin, ciprofloxacin and nitrofurantoin) account for just over 77% of consumption.

Table 7.13 The 10 most consumed agents – oral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Amoxicillin	4.25	4.25	4.25	4.25	4.25	4.25	4.25	4.25	4.25	4.25
Doxycycline	2.50	2.50	2.50	2.50	2.50	2.50	2.50	2.50	2.50	
Amoxicillin and enzyme inhibitor	2.36	2.36	2.36	2.36	2.36	2.36	2.36	2.36		
Azithromycin	1.54	1.54	1.54	1.54	1.54	1.54	1.54			
Ciprofloxacin	1.33	1.33	1.33	1.33	1.33	1.33				
Nitrofurantoin	1.01	1.01	1.01	1.01	1.01					
Clarithromycin	0.89	0.89	0.89	0.89						
Levofloxacin	0.38	0.38	0.38							
Ampicillin	0.37	0.37								
Cefalexin	0.25									
Total consumption for this group of agents	**14.90**	**14.64**	**14.27**	**13.89**	**12.99**	**11.98**	**10.65**	**9.11**	**6.75**	**4.25**
Total consumption for all oral J01 antibacterials	**16.71**	**16.71**	**16.71**	**16.71**	**16.71**	**16.71**	**16.71**	**16.71**	**16.71**	**16.71**
Proportion (%) of total consumption for oral J01 antibacterials	**89.2%**	**87.6%**	**85.4%**	**83.1%**	**77.8%**	**71.7%**	**63.7%**	**54.5%**	**40.4%**	**25.4%**

[a] DDD: daily defined dose.

7.5.2 The 10 most consumed agents – parenteral formulation

Table 7.14 summarizes consumption of the 10 most consumed parenteral agents in 2014. Four of these (ceftriaxone, cefotaxime, cefepime and cefazolin) account for almost 75% of consumption.

Table 7.14 The 10 most consumed agents – parenteral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Ceftriaxone	1.51	1.51	1.51	1.51	1.51	1.51	1.51	1.51	1.51	1.51
Cefotaxime	0.42	0.42	0.42	0.42	0.42	0.42	0.42	0.42	0.42	
Cefepime	0.38	0.38	0.38	0.38	0.38	0.38	0.38	0.38		
Cefazolin	0.14	0.14	0.14	0.14	0.14	0.14	0.14			
Levofloxacin	0.12	0.12	0.12	0.12	0.12	0.12				
Metronidazole	0.11	0.11	0.11	0.11	0.11					
Ciprofloxacin	0.11	0.11	0.11	0.11						
Amikacin	0.08	0.08	0.08							
Gentamicin	0.08	0.08								
Meropenem	0.06									
Total consumption for this group of agents	**3.00**	**2.94**	**2.87**	**2.79**	**2.68**	**2.57**	**2.45**	**2.31**	**1.93**	**1.51**
Total consumption for all parental J01 antibacterials	**3.28**	**3.28**	**3.28**	**3.28**	**3.28**	**3.28**	**3.28**	**3.28**	**3.28**	**3.28**
Proportion (%) of total consumption for parental J01 antibacterials	**91.5%**	**89.7%**	**87.4%**	**85.0%**	**81.6%**	**78.2%**	**74.6%**	**70.3%**	**58.9%**	**46.0%**

[a] DDD: daily defined dose.

7.6 Comments

The analyses presented in this chapter are based on sales records of wholesalers and local manufacturers, and the results suggest that import and medicine supply cycles may have a substantial impact on the estimates and explain (in part) the fluctuations between years.

8. KYRGYZSTAN

8.1 Data sources and years of data collection

Kyrgyzstan provided data for each of the four years of data collection (2011–2014). The main sources were import records provided by the drug agency and information provided by wholesalers (Table 8.1).

Table 8.1 Sources of data used for consumption estimates (2011–2014)

Year	Health care sector coverage	Data type	Data source (consumption)	Population	Data source (population)
2011	Total care	Import records Sales records	Drug agency Wholesalers	5 514 600	World Bank
2012	Total care	Import records Sales records	Drug agency Wholesalers	5 607 200	World Bank
2013	Total care	Import records Sales records	Drug agency Wholesalers	5 719 600	World Bank
2014	Total care	Import records Sales records	Drug agency Wholesalers	5 835 500	World Bank

8.2 Estimates of volumes of consumption of antibacterials for systemic use (J01)

Total consumption of antibacterials for systemic use (ATC class J01) is examined by route of administration (oral and parenteral formulations) and by pharmacological subgroup.

8.2.1 Total consumption of J01 antibacterials by route of administration

The consumption of oral and parenteral (injectable) formulations of J01 antibacterials is shown in Fig. 8.1 and summarized in Table 8.2 as DDD/1000 inhabitants per day (DID).

The substantial increase in total J01 consumption from 2011 to 2014 (24.0 to 36.8 DID) in part reflects the larger number of antibacterial preparations registered in Kyrgyzstan during the period.

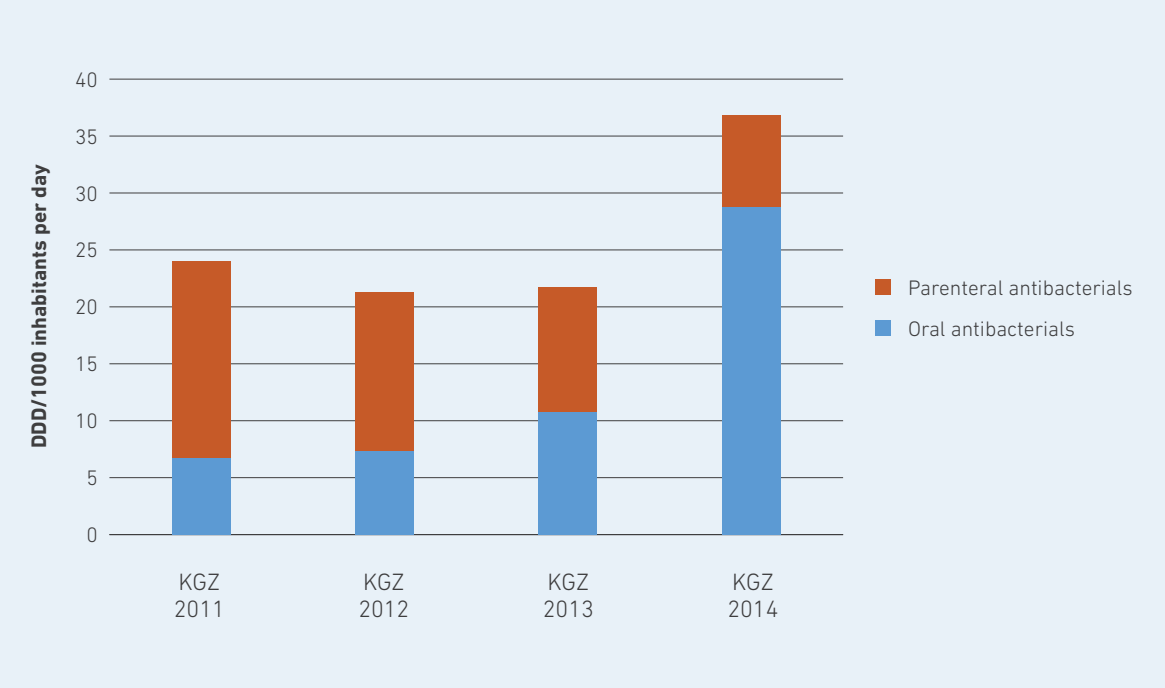

Fig. 8.1 Total consumption of J01 antibacterials by route of administration

DDD: defined daily dose.

Table 8.2 Total consumption of J01 antibacterials by route of administration

Route of administration	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Oral J01	6.7 (28)	7.3 (34)	10.7 (49)	28.7 (78)
Parenteral J01	17.3 (72)	14 (66)	11 (51)	8.1 (22)
Total	**24.0**	**21.3**	**21.7**	**36.8**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

The substantial reduction in proportion of consumption of parenteral antibacterials (72% to 22%) is the result of sustained activities undertaken by the Ministry of Health and the Mandatory Health Insurance Fund. During this time, clinical protocols for primary care were developed and implemented. These recommended the use of oral rather than parenteral forms of antibacterials. Compliance with these protocols was frequently checked. These regulatory measures were supported by the Association of Family Physicians and the Association of Hospitals, which conducted active training of doctors on rational prescribing of medicines. In addition, the Mandatory Health Insurance Fund undertook active interventions to reduce unnecessary hospitalizations of patients. Together, these interventions contributed to the changes in practice reflected in the consumption data.

8.2.2 Total consumption of J01 antibacterials by pharmacological subgroup

The consumption of J01 antibacterials by pharmacological subgroup is shown in Fig. 8.2 and summarized in Table 8.3.

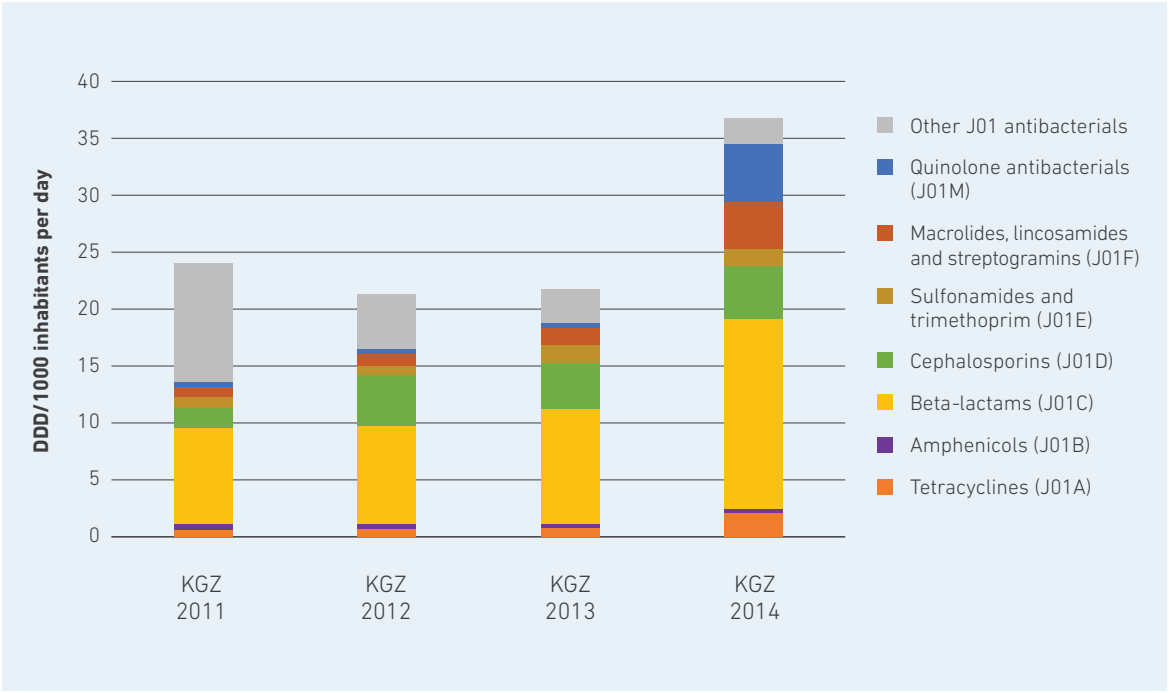

Fig. 8.2 Total consumption of J01 antibacterials by pharmacological subgroup

DDD: defined daily dose.

The volumes of consumption of most of the pharmacological subgroups increased over time: tetracyclines (J01A), beta-lactams (J01C), cephalosporins (J01D), macrolides, lincosamides and streptogramins (J01F) and quinolones (J01M).

Table 8.3 Total consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	DDD/1000 inhabitants per day[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	0.6	0.6	0.7	2.1
Amphenicols (J01B)	0.5	0.5	0.4	0.3
Beta-lactams (J01C)	8.5	8.6	10.1	16.7
Cephalosporins (J01D)	1.8	4.4	4.0	4.7
Sulfonamides and trimethoprim (J01E)	1.0	0.8	1.7	1.5
Macrolides, lincosamides and streptogramins (J01F)	0.8	1.1	1.5	4.1
Quinolone antibacterials (J01M)	0.5	0.4	0.4	5.0
Other J01 antibacterials (J01G, J01R, J01X)	10.4	4.8	3.0	2.4
Total[b]	**24.0**	**21.3**	**21.7**	**36.8**

[a] DDD: daily defined dose. [b] Total amounts may vary slightly owing to rounding.

8.3 Relative consumption of J01 antibacterials by subgroup

8.3.1 Relative consumption of J01 antibacterials by pharmacological subgroup

The relative consumption of pharmacological subgroups measured as a proportion of total J01 antibacterials is shown in Fig. 8.3 and summarized in Table 8.4.

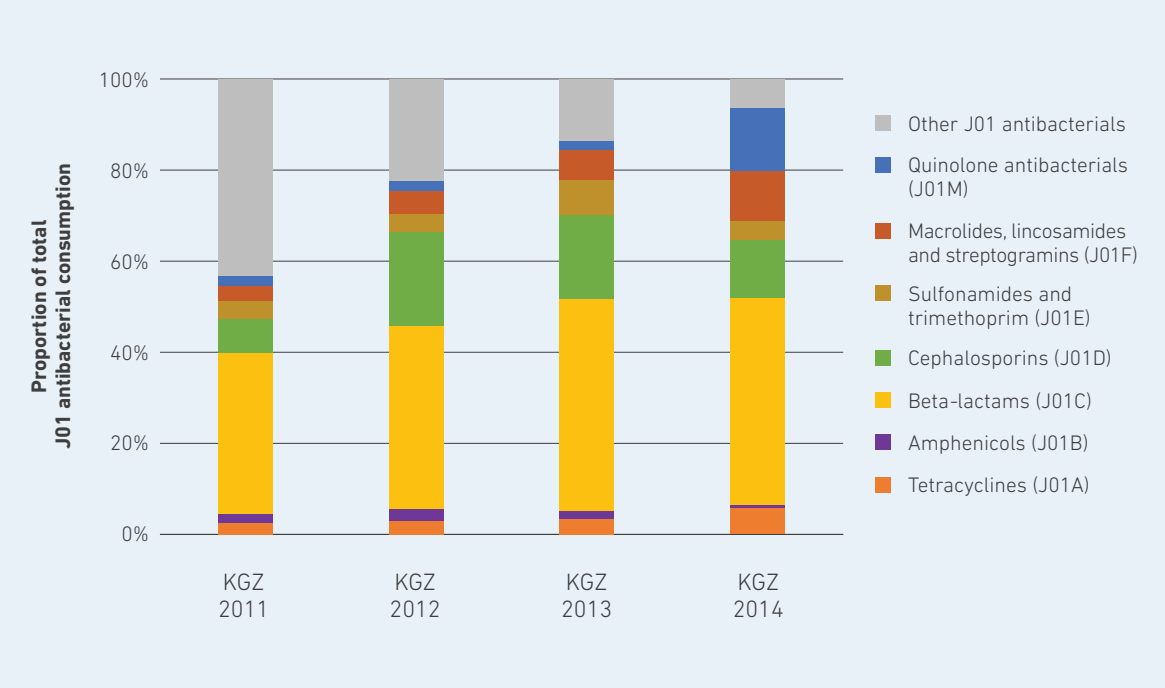

Fig. 8.3 Relative consumption of J01 antibacterials by pharmacological subgroup

There were substantial increases in the relative consumption of beta-lactams (J01C), which rose from 35.3% to 45.4%, cephalosporins (J01D), from 7.4% to 12.8%, macrolides, lincosamides and streptogramins (J01F), from 3.3% to 11.2%, and quinolones (J01M), from 2.1% to 13.7%. The most substantial reduction was in the "other J01 antibacterials" category, from 43.4% to 6.4% (Table 8.4).

Table 8.4 Relative consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	Consumption as proportion of total J01 consumption (%)[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	2.0	3.0	3.3	5.7
Amphenicols (J01B)	2.0	2.5	1.9	0.8
Beta-lactams (J01C)	35.3	40.2	46.4	45.4
Cephalosporins (J01D)	7.4	20.8	18.5	12.8
Sulfonamides and trimethoprim (J01E)	4.1	3.9	7.6	4.0
Macrolides, lincosamides and streptogramins (J01F)	3.3	5.0	6.7	11.2
Quinolone antibacterials (J01M)	2.1	2.1	1.9	13.7
Other J01 antibacterials (J01G, J01R, J01X)	43.4	22.5	13.8	6.4

[a] Total percentages may vary slightly owing to rounding.

8.3.2 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Cephalosporins and quinolones are broad-spectrum antibiotics and are considered second-line antibiotics in most prescribing guidelines. Generally, it is recommended that their use should be restricted to ensure availability as second-line therapy, should first-line antibiotics fail.

The relative consumption of cephalosporins and quinolones measured as a proportion of total J01 antibacterials is shown in Fig. 8.4 and summarized in Table 8.5.

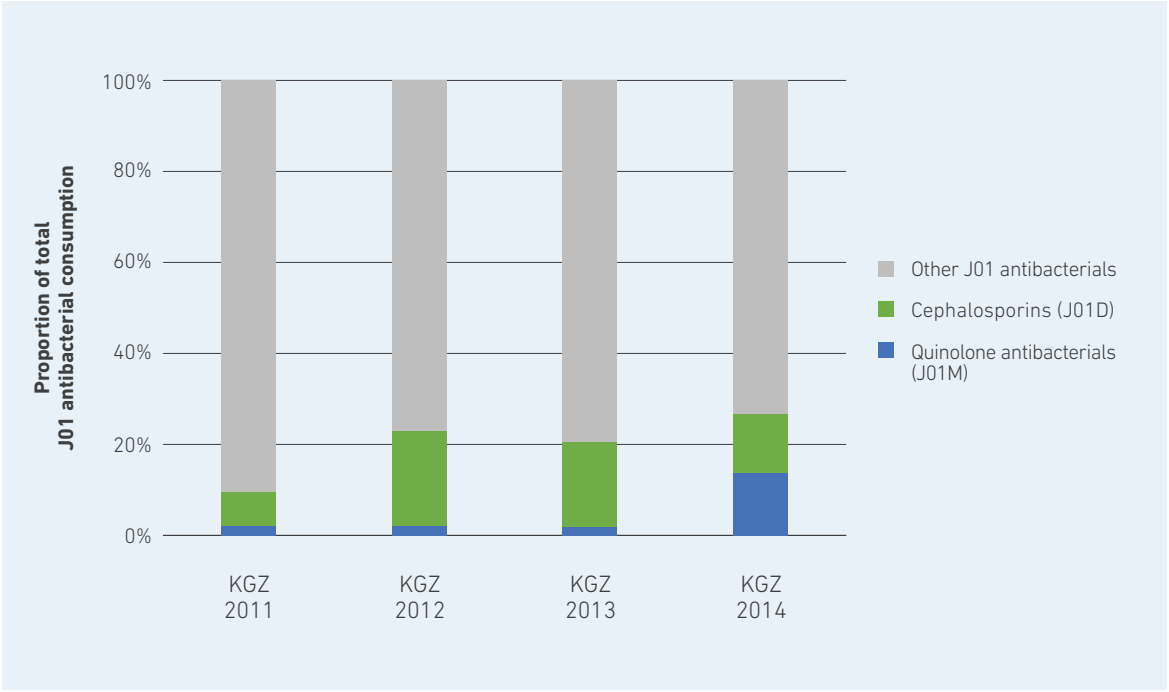

Fig. 8.4 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

The relative increases in consumption of both cephalosporins and quinolones over 2011–2014 were substantial. Together these two categories constituted 27% of J01 antibacterial consumption in 2014 (Table 8.5).

Table 8.5 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Class of antibacterial agents	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Quinolone antibacterials (J01M)	0.5 (2)	0.4 (2)	0.4 (2)	5 (14)
Cephalosporins (J01D)	1.8 (7)	4.4 (21)	4 (18)	4.7 (13)
Other J01 antibacterials	21.7 (91)	16.4 (77)	17.3 (80)	27.1 (73)
Total	**24.0**	**21.3**	**21.7**	**36.8**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

8.4 Relative consumption by choice of agent

8.4.1 Relative consumption of cephalosporins by generation

Third- and fourth-generation cephalosporins have a broader spectrum of activity than first- and second-generation agents, with enhanced coverage of both Gram-positive and Gram-negative organisms. WHO (2012) has identified third- and fourth-generation cephalosporins as some of the agents of highest priority for risk management to ensure that critically important antimicrobials are used prudently both in human and veterinary medicine.

The relative consumption of first-, second-, third- and fourth-generation cephalosporins in 2011–2014 is shown in Fig. 8.5 and summarized in Table 8.6.

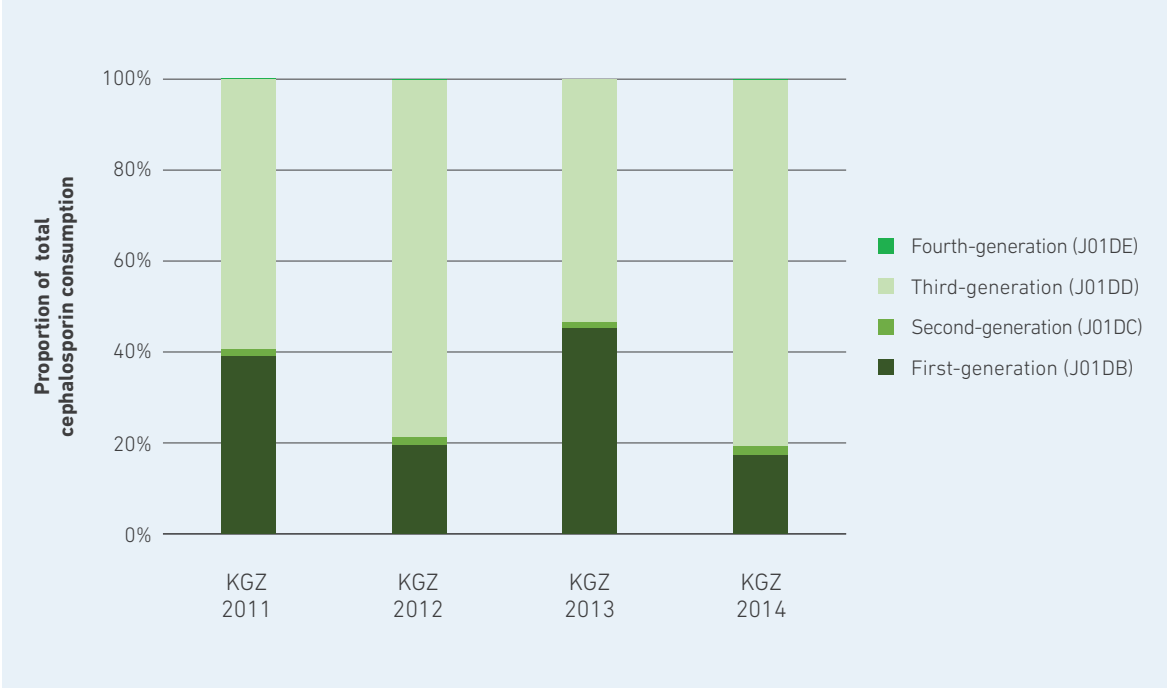

Fig. 8.5 Relative consumption of cephalosporins by generation

Consumption of both second- and fourth-generation cephalosporins over time was very limited. Most consumption was of third-generation agents (increasing from 59% in 2011 to 80% in 2014), matched by reductions in consumption of first-generation cephalosporins (39% in 2011 to 17% in 2014; Table 8.6).

Table 8.6 Relative consumption of cephalosporins by generation

Generation	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
First-generation (J01DB)	0.7 (39)	0.9 (19)	1.8 (45)	0.8 (17)
Second-generation (J01DC)	<0.1	<0.1	<0.1	0.1 (2)
Third-generation (J01DD)	1 (59)	3.5 (79)	2.1 (53)	3.8 (80)
Fourth-generation (J01DE)	<0.1	<0.1	<0.1	<0.1
Total	**1.8**	**4.4**	**4.0**	**4.7**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

8.4.1.1 Choice of first-generation cephalosporins (J01DB)

Table 8.7 summarizes the pattern of consumption of first-generation cephalosporins in 2011–2014. Cefazolin was the most consumed agent.

Table 8.7 Relative consumption of agents within first-generation cephalosporins (J01DB)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefalexin	<0.1	<0.1	<0.1	<0.1
Cefazolin	0.7 (100)	0.9 (100)	1.8 (100)	0.8 (100)
Total	**0.7**	**0.9**	**1.8**	**0.8**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

8.4.1.2 Choice of second-generation cephalosporins (J01DC)

Levels of consumption of second-generation cephalosporins were low in 2011–2014.

8.4.1.3 Choice of third-generation cephalosporins (J01DD)

Table 8.8 summarizes the pattern of consumption of third-generation cephalosporins in 2011–2014. Ceftriaxone was the most consumed agent.

Table 8.8 Relative consumption of agents within third-generation cephalosporins (J01DD)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefotaxime	<0.1	<0.1	<0.1	<0.1
Ceftazidime	<0.1	<0.1	<0.1	<0.1
Ceftriaxone	1 (92)	3.4 (98)	2 (93)	3.4 (90)
Cefixime	<0.1	<0.1	<0.1	0.3 (9)
Cefoperazone	<0.1	<0.1	<0.1	<0.1
Cefpodoxime	<0.1	<0.1	<0.1	<0.1
Cefoperazone, combinations	<0.1	<0.1	<0.1	<0.1
Total	**1.0**	**3.5**	**2.1**	**3.8**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

8.4.1.4 Choice of fourth-generation cephalosporins (J01DE)

Consumption of any of the fourth-generation cephalosporins was very limited.

8.4.2 Relative consumption of agents within fluoroquinolones (J01MA)

Quinolone antibacterials comprised around 14% of consumption of J01 antibacterials in 2014 (see Table 8.4). Almost all quinolone consumption was from the fluoroquinolone category (J01MA). The most consumed agents were ciprofloxacin and levofloxacin (Table 8.9).

Table 8.9 Relative consumption of agents within fluoroquinolones (J01MA)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Ofloxacin	<0.1	<0.1	<0.1	<0.1
Ciprofloxacin	0.3 (65)	0.1 (30)	0.1 (28)	2.3 (46)
Norfloxacin	0.1 (21)	0.2 (38)	0.1 (35)	0.2 (3)
Levofloxacin	<0.1	0.1 (24)	0.1 (26)	2.4 (48)
Moxifloxacin	<0.1	<0.1	<0.1	<0.1
Total	**0.5**	**0.4**	**0.4**	**5.0**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

8.4.3 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

The addition of clavulanic acid to amoxicillin extends the spectrum of activity of amoxicillin against beta-lactamase-producing bacteria. Amoxicillin and clavulanic acid is recommended as second-line treatment in many treatment guidelines.

Table 8.10 summarizes the relative consumption of amoxicillin and broader-spectrum amoxicillin and clavulanic acid. Reported consumption was almost exclusively amoxicillin between 2011 and 2013. In 2014, almost half of the consumption was amoxicillin and clavulanic acid.

Table 8.10 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Amoxicillin (J01CA04)	3.1 (100)	3.3 (100)	5.5 (100)	7.4 (51)
Amoxicillin and clavulanic acid (J01CR02)	<0.1	<0.1	<0.1	7.3 (49)
Total	**3.1**	**3.3**	**5.5**	**14.7**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

8.5 The 10 most consumed agents

While the number of J01 antibacterial agents available is large, there is considerable evidence from ESAC-Net and other analyses that consumption tends to be concentrated in a relatively small number.

8.5.1 The 10 most consumed agents – oral formulation

Table 8.11 summarizes consumption of the oral agents that comprise the 10 most consumed in 2014. Five agents (amoxicillin, amoxicillin and enzyme inhibitor, erythromycin, levofloxacin and ciprofloxacin) account for 77% of consumption.

Table 8.11 The 10 most consumed agents – oral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Amoxicillin	7.44	7.44	7.44	7.44	7.44	7.44	7.44	7.44	7.44	7.44
Amoxicillin and enzyme inhibitor	7.25	7.25	7.25	7.25	7.25	7.25	7.25	7.25	7.25	
Erythromycin	2.67	2.67	2.67	2.67	2.67	2.67	2.67	2.67		
Levofloxacin	2.42	2.42	2.42	2.42	2.42	2.42	2.42			
Ciprofloxacin	2.28	2.28	2.28	2.28	2.28	2.28				
Sulfamethoxazole and trimethoprim	1.48	1.48	1.48	1.48	1.48					
Doxycycline	1.27	1.27	1.27	1.27						
Azithromycin	1.06	1.06	1.06							
Tetracycline	0.83	0.83								
Nitrofurantoin	0.68									
Total consumption for this group of agents	**27.39**	**26.71**	**25.88**	**24.82**	**23.55**	**22.07**	**19.79**	**17.37**	**14.69**	**7.44**
Total consumption for all oral J01 antibacterials	**28.72**	**28.72**	**28.72**	**28.72**	**28.72**	**28.72**	**28.72**	**28.72**	**28.72**	**28.72**
Proportion (%) of total consumption for oral J01 antibacterials	**95.4%**	**93.0%**	**90.1%**	**86.4%**	**82.0%**	**76.8%**	**68.9%**	**60.5%**	**51.2%**	**25.9%**

[a] DDD: daily defined dose.

8.5.2 The 10 most consumed agents – parenteral formulation

Table 8.12 summarizes consumption of the 10 most consumed parenteral agents in 2014. Four of these (ceftriaxone, benzylpenicillin, kanamycin and ampicillin) account for just over 78% of consumption.

Table 8.12 The 10 most consumed agents – parenteral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Ceftriaxone	3.41	3.41	3.41	3.41	3.41	3.41	3.41	3.41	3.41	3.41
Benzylpenicillin	1.10	1.10	1.10	1.10	1.10	1.10	1.10	1.10	1.10	
Kanamycin	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01		
Ampicillin	0.85	0.85	0.85	0.85	0.85	0.85	0.85			
Cefazolin	0.81	0.81	0.81	0.81	0.81	0.81				
Metronidazole	0.28	0.28	0.28	0.28	0.28					
Streptomycin	0.17	0.17	0.17	0.17						
Chloramphenicol	0.11	0.11	0.11							
Gentamicin	0.10	0.10								
Cefuroxime	0.06									
Total consumption for this group of agents	**7.90**	**7.84**	**7.74**	**7.63**	**7.46**	**7.18**	**6.37**	**5.52**	**4.51**	**3.41**
Total consumption for all parental J01 antibacterials	**8.10**	**8.10**	**8.10**	**8.10**	**8.10**	**8.10**	**8.10**	**8.10**	**8.10**	**8.10**
Proportion (%) of total consumption for parental J01 antibacterials	**97.4%**	**96.7%**	**95.5%**	**94.1%**	**92.1%**	**88.6%**	**78.6%**	**68.1%**	**55.7%**	**42.1%**

[a] DDD: daily defined dose.

8.6 Comments

The analyses presented in this chapter are based on import records and sales records of wholesalers and local manufacturers, and the results suggest that import and medicine supply cycles may have a substantial impact on the estimates and explain (in part) the fluctuations between years. Further years of data are needed to determine whether levels of antibacterial consumption will continue to rise, as occurred in 2014.

9. MONTENEGRO

9.1 Data sources and years of data collection

Montenegro provided data for each of the four years of data collection (2011–2014). The main sources were sales records of wholesalers provided by the drug agency (Table 9.1).

Table 9.1 Sources of data used for consumption estimates (2011–2014)

Year	Health care sector coverage	Data type	Data source (consumption)	Population	Data source (population)
2011	Total care	Sales records of wholesalers	Drug agency	620 079	World Bank
2012	Total care	Sales records of wholesalers	Drug agency	620 601	World Bank
2013	Total care	Sales records of wholesalers	Drug agency	621 207	World Bank
2014	Total care	Sales records of wholesalers	Drug agency	621 810	World Bank

9.2 Estimates of volumes of consumption of antibacterials for systemic use (J01)

Total consumption of antibacterials for systemic use (ATC class J01) is examined by route of administration (oral and parenteral formulations) and by pharmacological subgroup.

9.2.1 Total consumption of J01 antibacterials by route of administration

The consumption of oral and parenteral (injectable) formulations of J01 antibacterials is shown in Fig. 9.1 and summarized in Table 9.2 as DDD/1000 inhabitants per day (DID).

The data show some fluctuations in total consumption of J01 antibacterials over time (38.3 DID in 2011 and 32.7 DID in 2014), but this might be explained in part by the cycles of supply from wholesalers for these medicines. It should also be noted that in 2012 Montenegro enforced controls on the supply of antibacterials as prescription-only medicines. The consumption estimates need to be interpreted in the light of this change.

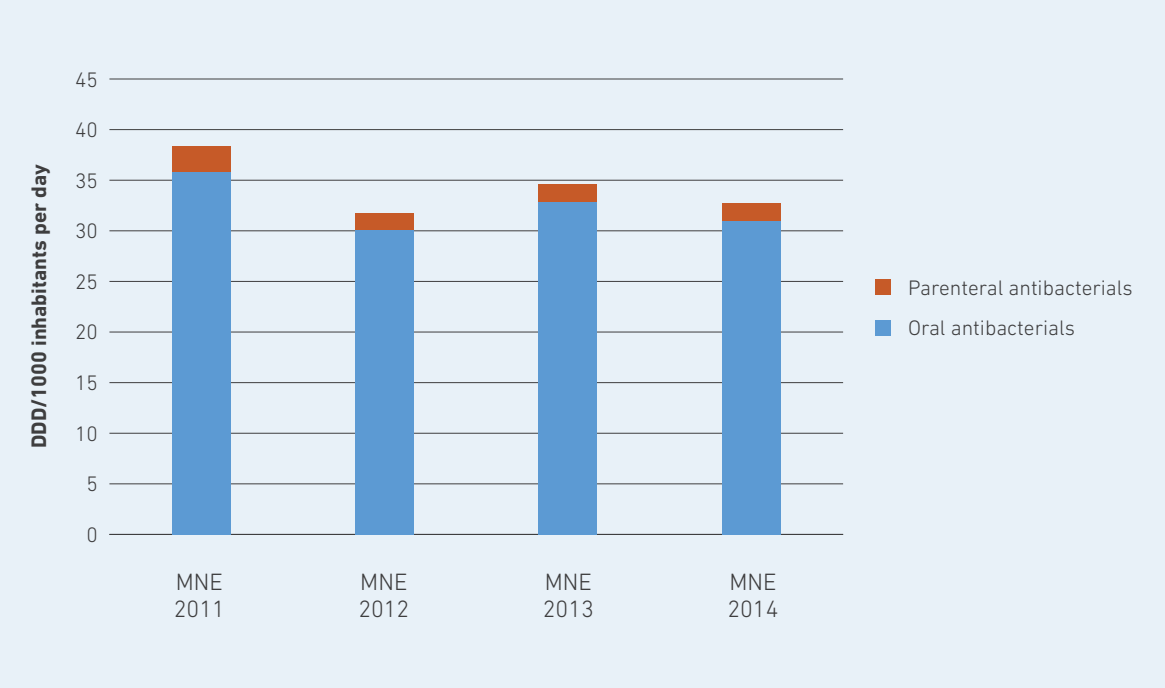

Fig. 9.1 Total consumption of J01 antibacterials by route of administration

DDD: defined daily dose.

The relative consumption of parenteral antibacterials was low in all years, comprising around 5% of total J01 consumption during 2011–2014 (Table 9.2).

Table 9.2 Total consumption of J01 antibacterials by route of administration

Route of administration	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Oral J01	35.8 (94)	30.1 (95)	32.8 (95)	31 (95)
Parenteral J01	2.5 (6)	1.7 (5)	1.7 (5)	1.7 (5)
Total	**38.3**	**31.8**	**34.6**	**32.7**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

9.2.2 Total consumption of J01 antibacterials by pharmacological subgroup

The consumption of J01 antibacterials by pharmacological subgroup is shown in Fig. 9.2 and summarized in Table 9.3.

The pattern of consumption among the pharmacological subgroups was similar during 2011–2014. The highest level of consumption was beta-lactams (J01C), at 15.4 DID in 2014 (Table 9.3).

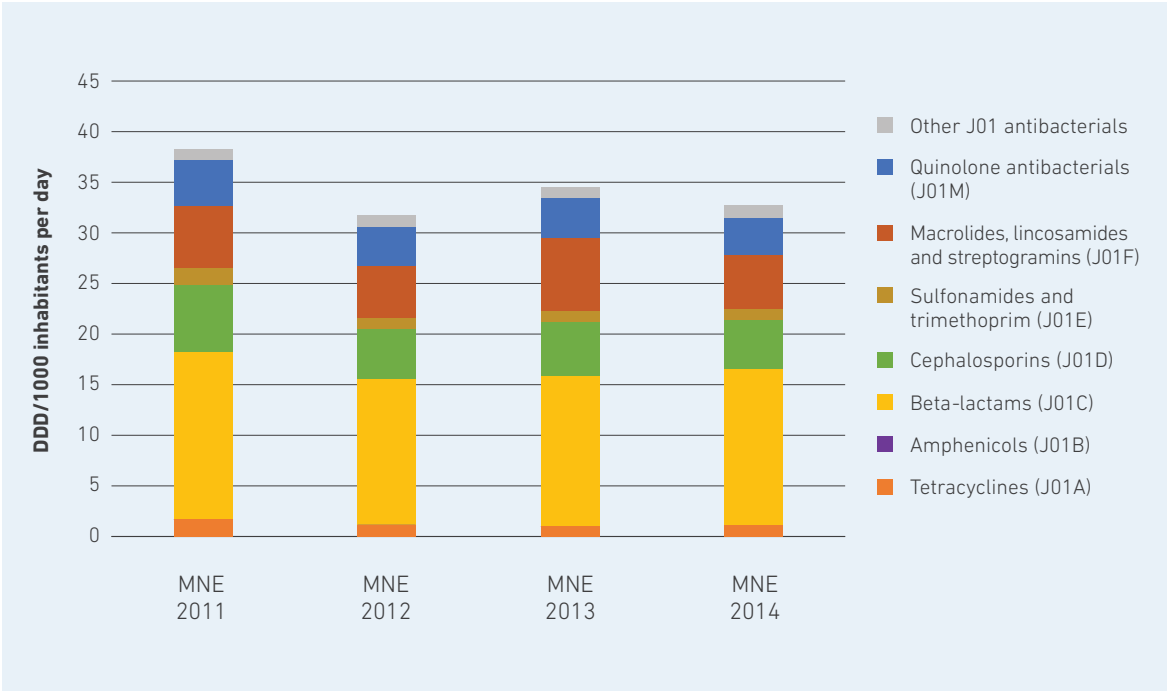

Fig. 9.2 Total consumption of J01 antibacterials by pharmacological subgroup

DDD: defined daily dose.

Table 9.3 Total consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	DDD/1000 inhabitants per day[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	1.7	1.2	1.0	1.1
Amphenicols (J01B)	<0.1	<0.1	<0.1	–
Beta-lactams (J01C)	16.4	14.4	14.7	15.4
Cephalosporins (J01D)	6.7	5.0	5.4	4.9
Sulfonamides and trimethoprim (J01E)	1.7	1.1	1.1	1.1
Macrolides, lincosamides and streptogramins (J01F)	6.2	5.2	7.2	5.3
Quinolone antibacterials (J01M)	4.5	3.9	3.9	3.7
Other J01 antibacterials (J01G, J01R, J01X)	1.1	1.2	1.2	1.2
Total[b]	**38.3**	**31.8**	**34.6**	**32.7**

[a] DDD: daily defined dose. [b] Total amounts may vary slightly owing to rounding.

9.3 Relative consumption of J01 antibacterials by subgroup

9.3.1 Relative consumption of J01 antibacterials by pharmacological subgroup

The relative consumption of pharmacological subgroups measured as a proportion of total J01 antibacterials is shown in Fig. 9.3 and summarized in Table 9.4.

Consumption of the subgroups was reasonably stable during 2011–2014, perhaps with some suggestion of increased consumption of beta-lactams (J01C), at 42.9% in 2011 and 47% in 2014, and decreased consumption of cephalosporins (J01D), at 17.4% in 2011 and 15% in 2014 (Table 9.4). These possible trends need to be confirmed with other data sources.

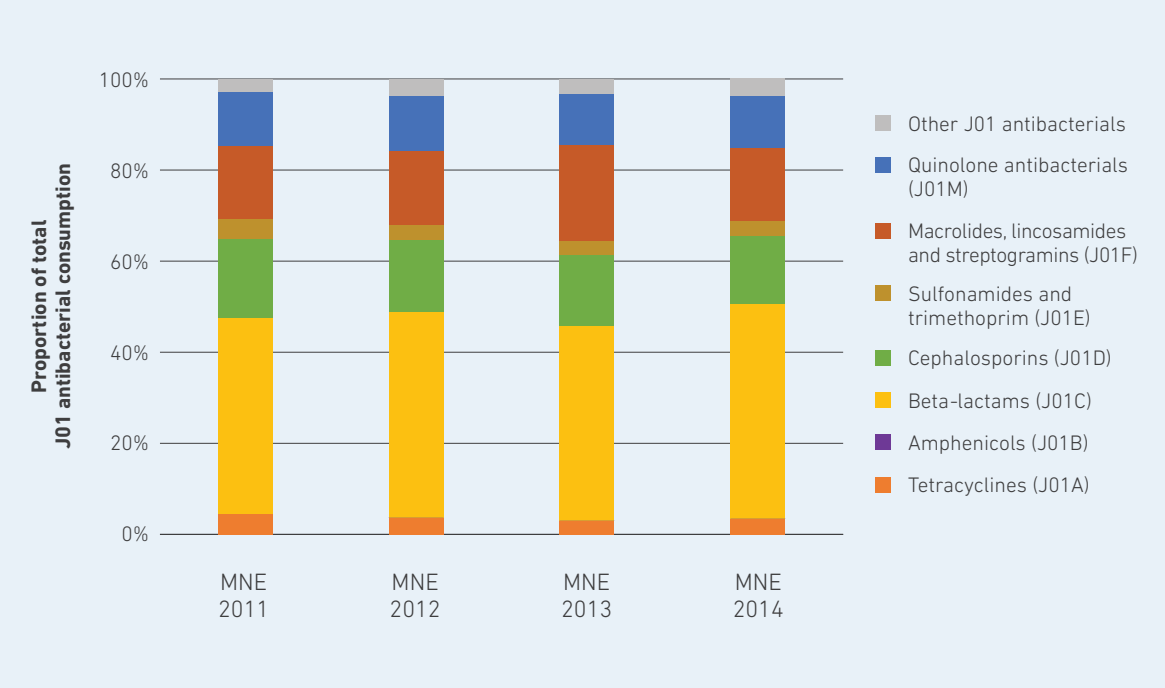

Fig. 9.3 Relative consumption of J01 antibacterials by pharmacological subgroup

Table 9.4 Relative consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	Consumption as proportion of total J01 consumption (%)[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	4.5	3.6	3.0	3.4
Amphenicols (J01B)	<0.1	<0.1	<0.1	–
Beta-lactams (J01C)	42.9	45.2	42.7	47.0
Cephalosporins (J01D)	17.4	15.7	15.6	15.0
Sulfonamides and trimethoprim (J01E)	4.4	3.4	3.2	3.3
Macrolides, lincosamides and streptogramins (J01F)	16.2	16.2	20.9	16.2
Quinolone antibacterials (J01M)	11.7	12.2	11.2	11.4
Other J01 antibacterials (J01G, J01R, J01X)	3.0	3.7	3.4	3.7

[a] Total percentages may vary slightly owing to rounding.

9.3.2 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Cephalosporins and quinolones are broad-spectrum antibiotics and are considered second-line antibiotics in most prescribing guidelines. Generally, it is recommended that their use should be restricted to ensure availability as second-line therapy, should first-line antibiotics fail.

The relative consumption of cephalosporins and quinolones measured as a proportion of total J01 antibacterials is shown in Fig. 9.4 and summarized in Table 9.5.

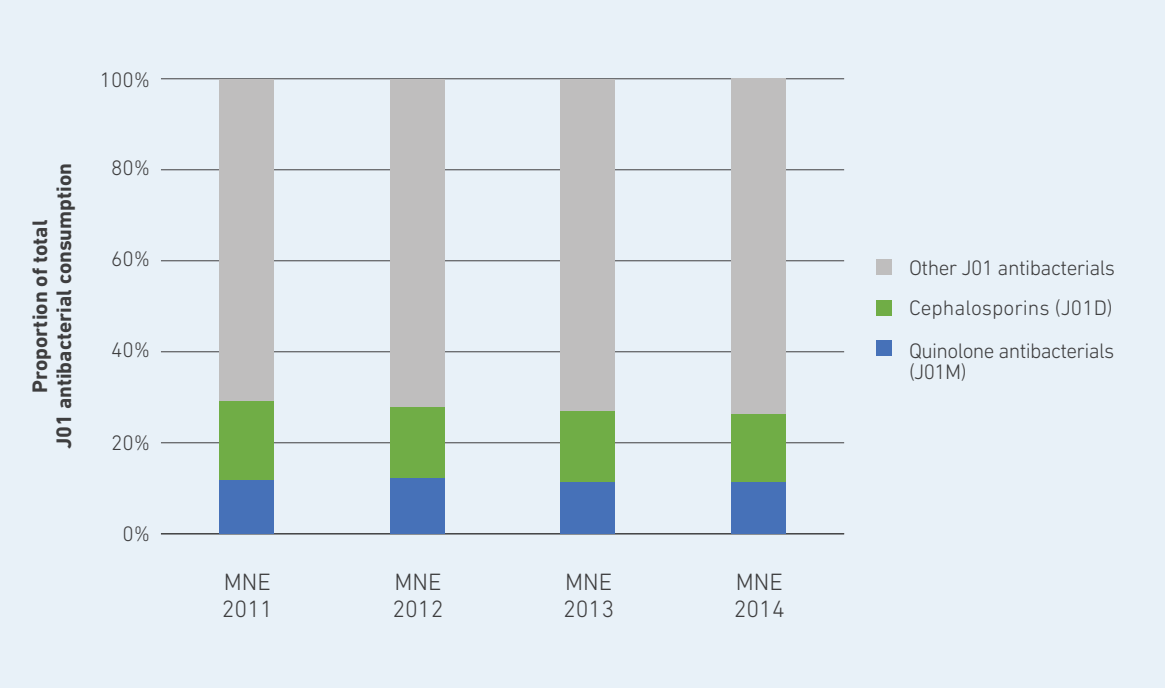

Fig. 9.4 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Consumption of quinolone antibacterials (J01M) was reasonably stable in 2011–2014 (11–12% of total consumption), while consumption of cephalosporins (J01D) decreased slightly over the period. Together these two subgroups comprised 26% of total J01 consumption in 2014 (Table 9.5).

Table 9.5 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Class of antibacterial agents	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Quinolone antibacterials (J01M)	4.5 (12)	3.9 (12)	3.9 (11)	3.7 (11)
Cephalosporins (J01D)	6.7 (17)	5 (16)	5.4 (16)	4.9 (15)
Other J01 antibacterials	27.2 (71)	22.9 (72)	25.3 (73)	24.1 (74)
Total	**38.3**	**31.8**	**34.6**	**32.7**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

9.4 Relative consumption by choice of agent

9.4.1 Relative consumption of cephalosporins by generation

Third- and fourth-generation cephalosporins have a broader spectrum of activity than first- and second-generation agents, with enhanced coverage of both Gram-positive and Gram-negative organisms. WHO (2012) has identified third- and fourth-generation cephalosporins as some of the agents of highest priority for risk management to ensure that critically important antimicrobials are used prudently both in human and veterinary medicine.

The relative consumption of first-, second-, third- and fourth-generation cephalosporins in 2011–2014 is shown in Fig. 9.5 and summarized in Table 9.6.

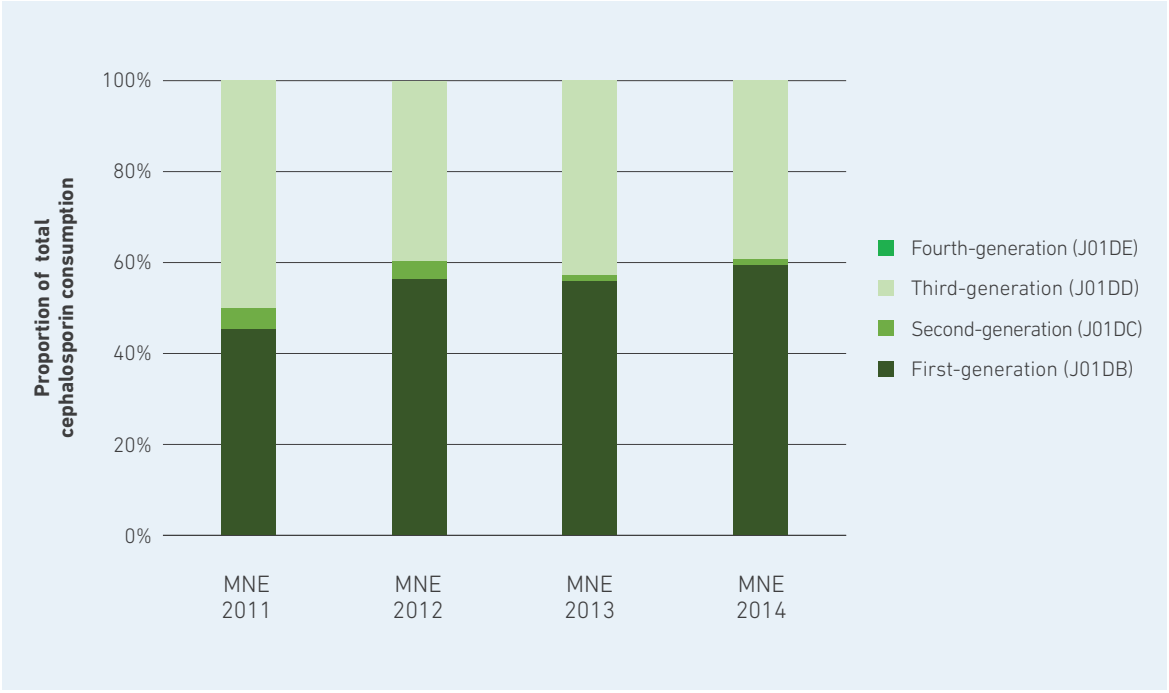

Fig. 9.5 Relative consumption of cephalosporins by generation

Consumption of fourth-generation cephalosporins during 2011–2014 was very limited (< 0.1 DID). Consumption of first-generation cephalosporins increased from 45% to 59% and a relative decrease from 50% to 39% in consumption of third-generation cephalosporins was reported.

Table 9.6 Relative consumption of cephalosporins by generation

Generation	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
First-generation (J01DB)	3 (45)	2.8 (56)	3 (56)	2.9 (59)
Second-generation (J01DC)	0.3 (5)	0.2 (4)	<0.1	<0.1
Third-generation (J01DD)	3.3 (50)	1.9 (40)	2.3 (43)	1.9 (39)
Fourth-generation (J01DE)	<0.1	<0.1	<0.1	<0.1
Total	**6.6**	**4.9**	**5.3**	**4.9**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

9.4.1.1 Choice of first-generation cephalosporins (J01DB)

Table 9.7 illustrates the pattern of consumption of first-generation cephalosporins in 2011–2014. Cefalexin was the most consumed agent.

Table 9.7 Relative consumption of agents within first-generation cephalosporins (J01DB)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefalexin	3 (99)	2.8 (99)	2.9 (99)	2.8 (98)
Cefazolin	<0.1	<0.1	<0.1	<0.1
Cefadroxil	<0.1	<0.1	<0.1	–
Total	**3.0**	**2.8**	**3.0**	**2.9**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

9.4.1.2 Choice of second-generation cephalosporins (J01DC)

Levels of consumption of the second-generation cephalosporins (cefuroxime, cefaclor) were low in 2011–2014.

9.4.1.3 Choice of third-generation cephalosporins (J01DD)

Table 9.8 summarizes the pattern of consumption of third-generation cephalosporins in 2011–2014. Cefixime was the most consumed agent.

Table 9.8 Relative consumption of agents within third-generation cephalosporins (J01DD)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Ceftazidime	<0.1	<0.1	<0.1	<0.1
Ceftriaxone	1.1 (33)	0.2 (11)	0.3 (13)	0.1 (6)
Cefixime	2.2 (66)	1.7 (87)	1.9 (85)	1.7 (90)
Cefpodoxime	–	<0.1	<0.1	<0.1
Ceftibuten	<0.1	<0.1	<0.1	<0.1
Total	**3.3**	**1.9**	**2.3**	**1.9**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

9.4.1.4 Choice of fourth-generation cephalosporins (J01DE)

Consumption of the fourth-generation cephalosporins was low in 2011–2014, with only cefpirome consumed in small amounts.

9.4.2 Relative consumption of agents within fluoroquinolones (J01MA)

Quinolone antibacterials comprised 11–12% of J01 antibacterials during 2011–2014 (see Table 9.4). Around 63% of quinolone consumption was from the fluoroquinolone category (J01MA). The most consumed agent was ciprofloxacin (Table 9.9).

Pipemidic acid was the agent from the "other quinolones" category (J01MB) that accounted for the remaining consumption (1.38 DID in 2014). Pipemidic acid is structurally similar to nalidixic acid and can be used in the treatment of urinary tract infections.

Table 9.9 Relative consumption of agents within fluoroquinolones (J01MA)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Ofloxacin	<0.1	<0.1	<0.1	<0.1
Ciprofloxacin	2.8 (95)	2.5 (96)	2.4 (95)	2.2 (95)
Norfloxacin	<0.1	<0.1	<0.1	<0.1
Levofloxacin	<0.1	<0.1	<0.1	<0.1
Moxifloxacin	<0.1	<0.1	<0.1	<0.1
Total	**3.0**	**2.6**	**2.5**	**2.3**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

9.4.3 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

The addition of clavulanic acid to amoxicillin extends the spectrum of activity of amoxicillin against beta-lactamase-producing bacteria. Amoxicillin and clavulanic acid is recommended as second-line treatment in many treatment guidelines.

Table 9.10 summarizes the relative consumption of amoxicillin and broader-spectrum amoxicillin and clavulanic acid. Amoxicillin was the more consumed agent in all years reported.

Table 9.10 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Amoxicillin (J01CA04)	9.3 (65)	8.9 (67)	9.6 (69)	9.8 (70)
Amoxicillin and clavulanic acid (J01CR02)	5 (35)	4.4 (33)	4.2 (31)	4.3 (30)
Total	**14.2**	**13.2**	**13.8**	**14.1**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

9.5 The 10 most consumed agents

While the number of J01 antibacterial agents available is large, there is considerable evidence from ESAC-Net and other analyses that consumption tends to be concentrated in a relatively small number.

9.5.1 The 10 most consumed agents – oral formulation

Table 9.11 summarizes consumption of the oral agents that comprise the 10 most consumed in 2014. Six agents (amoxicillin, amoxicillin and enzyme inhibitor, azithromycin, cefalexin, ciprofloxacin and cefixime) account for just over 76% of consumption.

9.5.2 The 10 most consumed agents – parenteral formulation

Table 9.12 summarizes consumption of the 10 most consumed parenteral agents in 2014. Four of these (gentamicin, combinations of antibacterials, amikacin and ceftriaxone) account for just over 75% of consumption. Gentamicin alone accounted for 49% of consumption.

Table 9.11 The 10 most consumed agents – oral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Amoxicillin	9.77	9.77	9.77	9.77	9.77	9.77	9.77	9.77	9.77	9.77
Amoxicillin and enzyme inhibitor	4.29	4.29	4.29	4.29	4.29	4.29	4.29	4.29	4.29	
Azithromycin	2.99	2.99	2.99	2.99	2.99	2.99	2.99	2.99		
Cefalexin	2.83	2.83	2.83	2.83	2.83	2.83	2.83			
Ciprofloxacin	2.15	2.15	2.15	2.15	2.15	2.15				
Cefixime	1.71	1.71	1.71	1.71	1.71					
Erythromycin	1.62	1.62	1.62	1.62						
Pipemidic acid	1.37	1.37	1.37							
Sulfamethoxazole and trimethoprim	1.08	1.08								
Doxycycline	1.01									
Total consumption for this group of agents	**28.81**	**27.80**	**26.72**	**25.35**	**23.73**	**22.02**	**19.87**	**17.04**	**14.05**	**9.77**
Total consumption for all oral J01 antibacterials	**31.00**	**31.00**	**31.00**	**31.00**	**31.00**	**31.00**	**31.00**	**31.00**	**31.00**	**31.00**
Proportion (%) of total consumption for oral J01 antibacterials	**92.9%**	**89.7%**	**86.2%**	**81.8%**	**76.5%**	**71.0%**	**64.1%**	**55.0%**	**45.3%**	**31.5%**

[a] DDD: daily defined dose.

Table 9.12 The 10 most consumed agents – parenteral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Gentamicin	0.83	0.83	0.83	0.83	0.83	0.83	0.83	0.83	0.83	0.83
Combinations[b]	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	
Amikacin	0.16	0.16	0.16	0.16	0.16	0.16	0.16	0.16		
Ceftriaxone	0.11	0.11	0.11	0.11	0.11	0.11	0.11			
Metronidazole	0.08	0.08	0.08	0.08	0.08	0.08				
Ciprofloxacin	0.06	0.06	0.06	0.06	0.06					
Cefazolin	0.05	0.05	0.05	0.05						
Meropenem	0.05	0.05	0.05							
Ceftazidime	0.04	0.04								
Vancomycin	0.03									
Total consumption for this group of agents	**1.61**	**1.58**	**1.54**	**1.49**	**1.44**	**1.37**	**1.29**	**1.18**	**1.03**	**0.83**
Total consumption for all parental J01 antibacterials	**1.72**	**1.72**	**1.72**	**1.72**	**1.72**	**1.72**	**1.72**	**1.72**	**1.72**	**1.72**
Proportion (%) of total consumption for parental J01 antibacterials	**93.7%**	**92.0%**	**89.4%**	**86.7%**	**83.8%**	**80.1%**	**75.2%**	**68.9%**	**59.7%**	**48.6%**

[a] DDD: daily defined dose. [b] Combinations of antibacterials are: J01CA20, J01CE30, J01EB20, J01EC20 or J01ED20.

9.6 Comments

Interpretation of the data presented in this chapter relies on an understanding of the national context. The analyses are based on wholesaler records, and the results suggest that supply cycles may have an impact on the estimates and explain (in part) the fluctuations between years.

A more detailed understanding of the patterns of antimicrobial consumption would identify areas for further investigation and allow development of targeted interventions to address potential problems identified in the consumption of antibacterials.

10. REPUBLIC OF MOLDOVA

10.1 Data sources and years of data collection

The Republic of Moldova provided data for each of the four years of data collection (2011–2014). The main sources were import records provided by the drug agency and information provided by local pharmaceutical manufacturers (Table 10.1). Further information on the estimates provided by local manufacturers was not available.

Table 10.1 Sources of data used for consumption estimates (2011–2014)

Year	Health care sector coverage	Data type	Data source (consumption)	Population	Data source (population)
2011	Total care	Import records Manufacturing records	Drug agency Local manufacturers	3 559 986	World Bank
2012	Total care	Import records Manufacturing records	Drug agency Local manufacturers	3 559 519	World Bank
2013	Total care	Import records Manufacturing records	Drug agency Local manufacturers	3 558 566	World Bank
2014	Total care	Import records Manufacturing records	Drug agency Local manufacturers	3 556 397	World Bank

10.2 Estimates of volumes of consumption of antibacterials for systemic use (J01)

Total consumption of antibacterials for systemic use (ATC class J01) is examined by route of administration (oral and parenteral formulations) and by pharmacological subgroup.

10.2.1 Total consumption of J01 antibacterials by route of administration

The consumption of oral and parenteral (injectable) formulations of J01 antibacterials is shown in Fig. 10.1 and summarized in Table 10.2 as DDD/1000 inhabitants per day (DID).

The import data, supplemented with local manufacturer data, show considerable fluctuations in total consumption of J01 antibacterials over time, from 21.3 DID in 2011 to 17.7 DID in 2014,

with highest reported consumption of 22.8 DID in 2013. This pattern suggests there is some impact of the data sources used and might be explained in part by import and medicine supply cycles for these medicines.

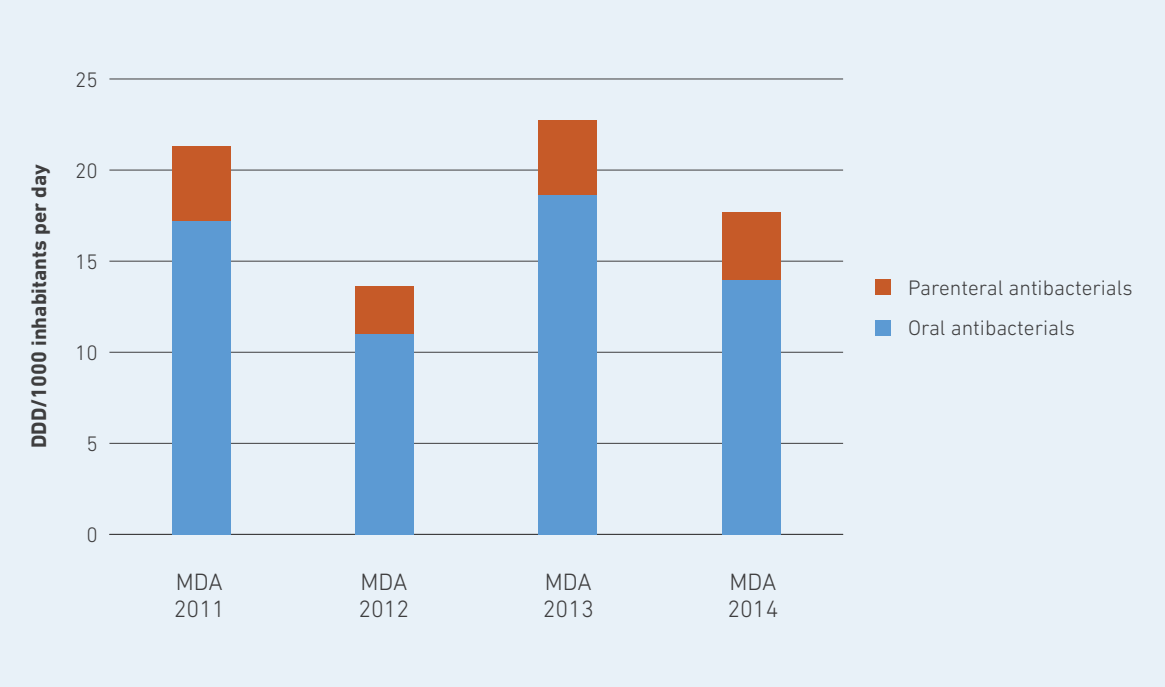

Fig. 10.1 Total consumption of J01 antibacterials by route of administration

DDD: defined daily dose.

The relative consumption of parenteral antibacterials remained reasonably stable at around 19% of total J01 consumption (Table 10.2).

Table 10.2 Total consumption of J01 antibacterials by route of administration

Route of administration	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Oral J01	17.2 (81)	11 (81)	18.6 (82)	14 (79)
Parenteral J01	4.1 (19)	2.6 (19)	4.1 (18)	3.7 (21)
Total	**21.3**	**13.6**	**22.8**	**17.7**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

10.2.2 Total consumption of J01 antibacterials by pharmacological subgroup

The consumption of J01 antibacterials by pharmacological subgroup is shown in Fig. 10.2 and summarized in Table 10.3.

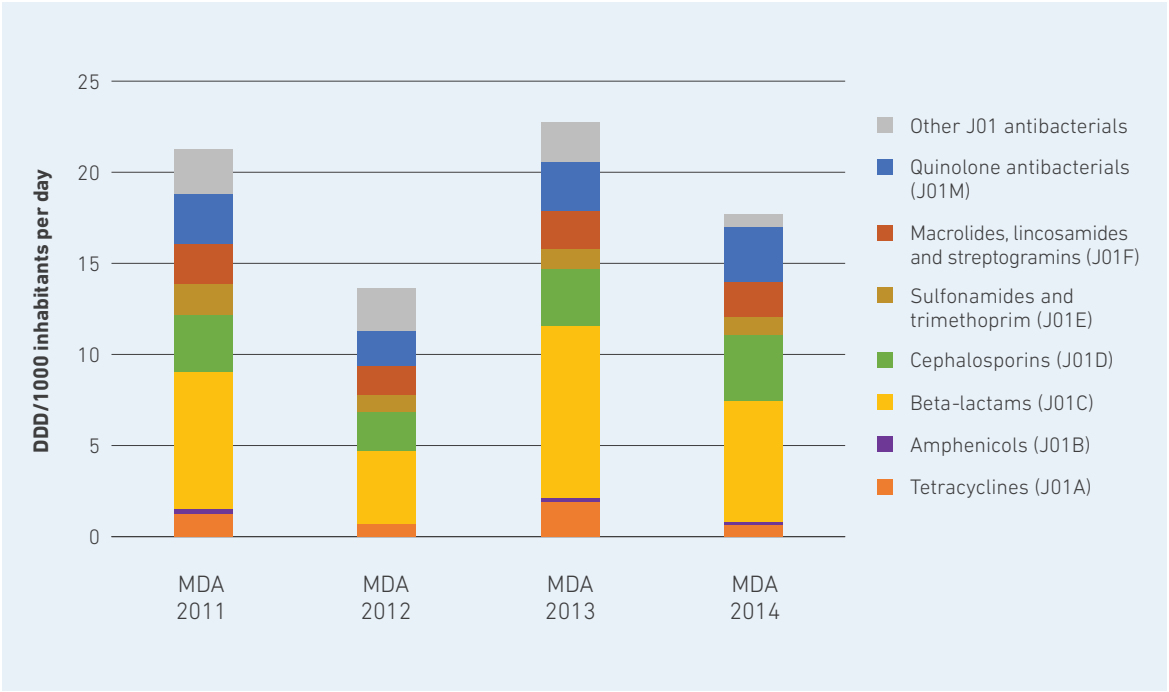

Fig. 10.2 Total consumption of J01 antibacterials by pharmacological subgroup

DDD: defined daily dose.

Given the fluctuations across the years it is difficult to draw substantial conclusions on changes in consumption for particular subgroups. Nevertheless, the data suggest some reductions in consumption of tetracyclines (J01A), which fell from 1.2 DID in 2011 to 0.6 DID in 2014, and sulfonamides and trimethoprim (J01E), which fell from 1.7 DID in 2011 to 1 DID in 2014. In 2014 the highest levels of consumption were beta-lactams (J01C), at 6.6 DID, and cephalosporins (J01D), at 3.7 DID (Table 10.3).

Table 10.3 Total consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	DDD/1000 inhabitants per day[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	1.2	0.7	1.9	0.6
Amphenicols (J01B)	0.2	<0.1	0.2	0.2
Beta-lactams (J01C)	7.5	4.0	9.5	6.6
Cephalosporins (J01D)	3.2	2.1	3.1	3.7
Sulfonamides and trimethoprim (J01E)	1.7	0.9	1.1	1.0
Macrolides, lincosamides and streptogramins (J01F)	2.2	1.6	2.1	1.9
Quinolone antibacterials (J01M)	2.7	1.9	2.7	3.0
Other J01 antibacterials (J01G, J01R, J01X)	2.5	2.4	2.2	0.7
Total[b]	**21.3**	**13.6**	**22.8**	**17.7**

[a] DDD: daily defined dose. [b] Total amounts may vary slightly owing to rounding.

10.3 Relative consumption of J01 antibacterials by subgroup

10.3.1 Relative consumption of J01 antibacterials by pharmacological subgroup

The relative consumption of pharmacological subgroups measured as a proportion of total J01 antibacterials is shown in Fig. 10.3 and summarized in Table 10.4.

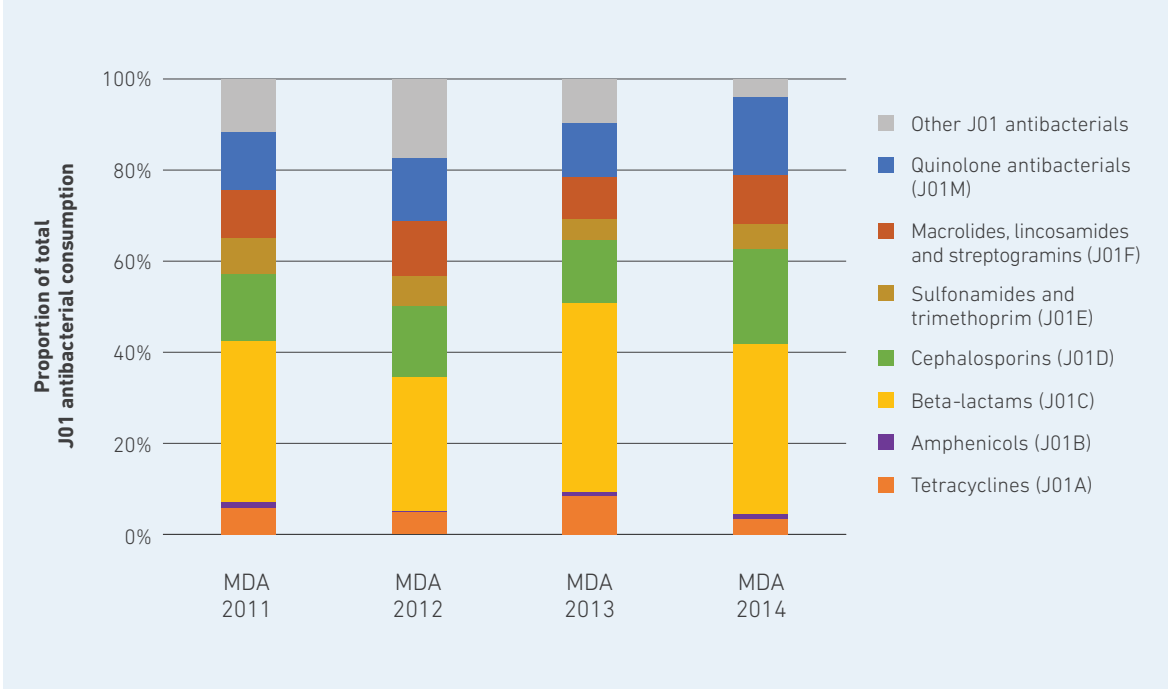

Fig. 10.3 Relative consumption of J01 antibacterials by pharmacological subgroup

The data illustrate the fluctuating patterns of consumption of the various subgroups over time. Most notable and consistent are the increasing relative consumption of cephalosporins (14.8% of J01 antibacterials consumption in 2011 and 20.7% in 2014) and quinolone antibacterials (12.7% in 2011 and 17% in 2014).

Table 10.4 Relative consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	Consumption as proportion of total J01 consumption (%)[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	5.8	4.8	8.4	3.4
Amphenicols (J01B)	1.1	0.4	0.7	1.0
Beta-lactams (J01C)	35.3	29.2	41.7	37.3
Cephalosporins (J01D)	14.8	15.7	13.7	20.7
Sulfonamides and trimethoprim (J01E)	7.9	6.7	4.7	5.6
Macrolides, lincosamides and streptogramins (J01F)	10.4	11.9	9.2	10.9
Quinolone antibacterials (J01M)	12.7	13.9	12.1	17.0
Other J01 antibacterials (J01G, J01R, J01X)	11.8	17.4	9.6	4.0

[a] Total percentages may vary slightly owing to rounding.

10.3.2 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Cephalosporins and quinolones are broad-spectrum antibiotics and are considered second-line antibiotics in most prescribing guidelines. Generally, it is recommended that their use should be restricted to ensure availability as second-line therapy, should first-line antibiotics fail.

The relative consumption of cephalosporins and quinolones measured as a proportion of total J01 antibacterials is shown in Fig. 10.4 and summarized in Table 10.5.

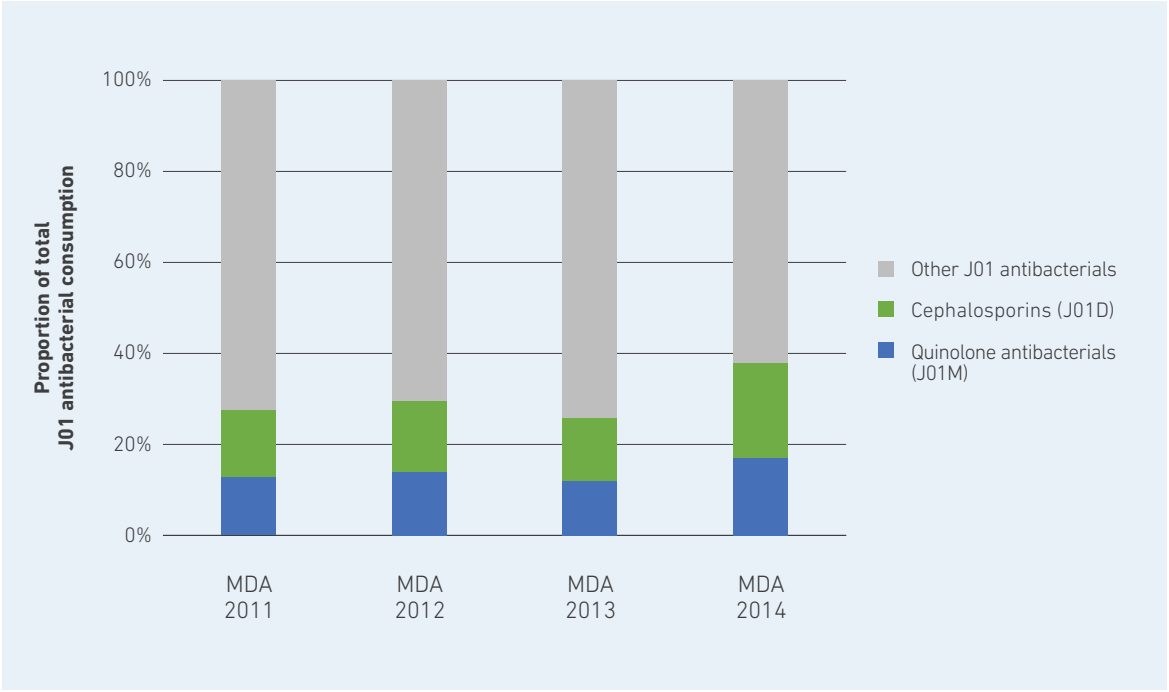

Fig. 10.4 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

These data suggest increasing relative consumption of cephalosporins and quinolone antibacterials over time, with the two groups comprising 38% of total J01 consumption in 2014 (Table 10.5). Given the fluctuations in annual J01 consumption estimates, these observations require confirmation using other data sources.

Table 10.5 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Class of antibacterial agents	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Quinolone antibacterials (J01M)	2.7 (13)	1.9 (14)	2.7 (12)	3 (17)
Cephalosporins (J01D)	3.2 (15)	2.1 (16)	3.1 (14)	3.7 (21)
Other J01 antibacterials	15.4 (72)	9.6 (70)	16.9 (74)	11 (62)
Total	**21.3**	**13.6**	**22.8**	**17.7**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

10.4 Relative consumption by choice of agent

10.4.1 Relative consumption of cephalosporins by generation

Third- and fourth-generation cephalosporins have a broader spectrum of activity than first- and second-generation agents, with enhanced coverage of both Gram-positive and Gram-negative organisms. WHO (2012) has identified third- and fourth-generation cephalosporins as some of the agents of highest priority for risk management to ensure that critically important antimicrobials are used prudently both in human and veterinary medicine.

The relative consumption of first-, second-, third- and fourth-generation cephalosporins in 2011–2014 is shown in Fig. 10.5 and summarized in Table 10.6.

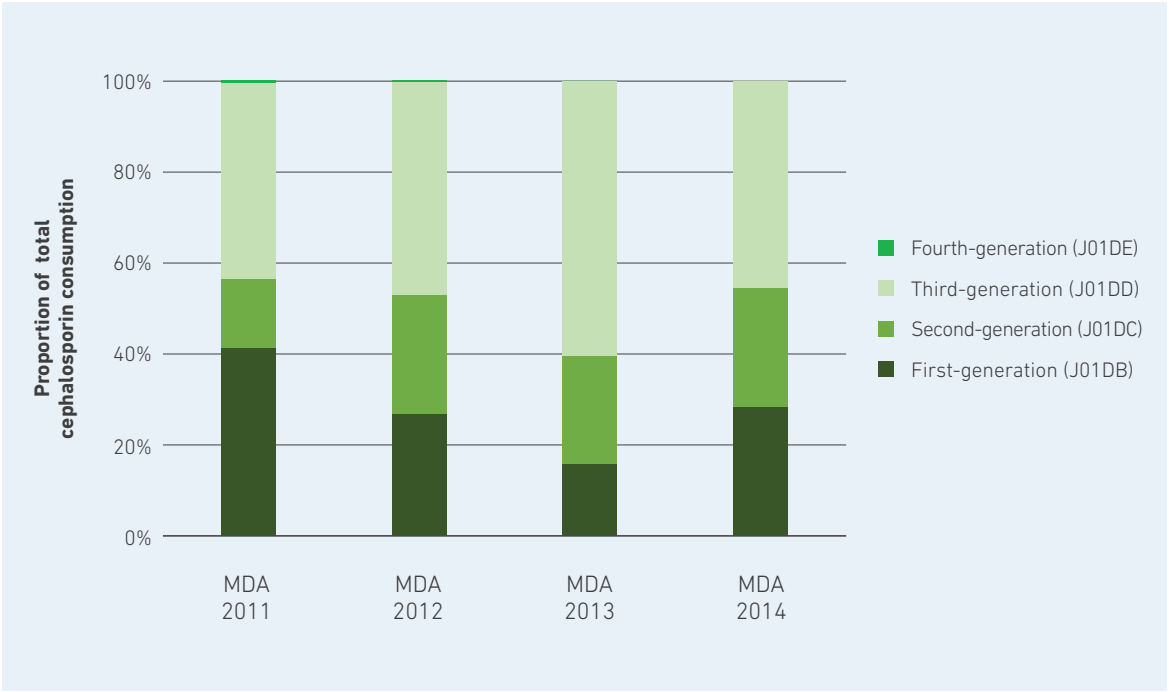

Fig. 10.5 Relative consumption of cephalosporins by generation

Consumption of fourth-generation cephalosporins was very limited (<0.1 DID) during 2011–2014, with reasonably stable consumption of third-generation agents (45% of total cephalosporin consumption in 2014; Table 10.6).

Table 10.6 Relative consumption of cephalosporins by generation

Generation	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
First-generation (J01DB)	1.3 (41)	0.6 (27)	0.5 (16)	1 (28)
Second-generation (J01DC)	0.5 (15)	0.6 (26)	0.7 (24)	1 (26)
Third-generation (J01DD)	1.4 (43)	1 (47)	1.9 (61)	1.7 (45)
Fourth-generation (J01DE)	<0.1	<0.1	<0.1	<0.1
Total	**3.2**	**2.1**	**3.1**	**3.7**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

10.4.1.1 Choice of first-generation cephalosporins (J01DB)

Table 10.7 illustrates the pattern of consumption of first-generation cephalosporins in 2011–2014. Cefalexin and cefazolin were those most consumed.

Table 10.7 Relative consumption of agents within first-generation cephalosporins (J01DB)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefalexin	0.5 (36)	0.2 (28)	0.2 (38)	0.3 (34)
Cefazolin	0.8 (64)	0.4 (72)	0.3 (62)	0.7 (66)
Total	**1.3**	**0.6**	**0.5**	**1.0**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

10.4.1.2 Choice of second-generation cephalosporins (J01DC)

Table 10.8 summarizes the pattern of consumption of second-generation cephalosporins in 2011–2014. Cefuroxime was the most consumed agent.

Table 10.8 Relative consumption of agents within second-generation cephalosporins (J01DC)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefuroxime	0.5 (96)	0.5 (86)	0.7 (99)	0.9 (90)
Cefaclor	<0.1	<0.1	<0.1	<0.1
Cefprozil	<0.1	<0.1	<0.1	<0.1
Total	**0.5**	**0.6**	**0.7**	**1.0**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

10.4.1.3 Choice of third-generation cephalosporins (J01DD)

Table 10.9 summarizes the pattern of consumption of third-generation cephalosporins in 2011–2014. Ceftriaxone was the most frequently consumed agent, with lower consumption of cefotaxime and cefixime.

Table 10.9 Relative consumption of agents within third-generation cephalosporins (J01DD)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefotaxime	0.2 (12)	<0.1	0.2 (13)	0.2 (11)
Ceftazidime	0.1 (8)	<0.1	<0.1	<0.1
Ceftriaxone	0.9 (66)	0.7 (69)	1.3 (75)	1.1 (66)
Cefixime	0.2 (12)	0.2 (19)	0.1 (6)	0.2 (10)
Cefoperazone	<0.1	<0.1	<0.1	<0.1
Cefpodoxime	–	–	–	<0.1
Ceftibuten	<0.1	<0.1	<0.1	<0.1
Cefdinir	–	–	–	<0.1
Total	**1.3**	**1.0**	**1.8**	**1.6**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

10.4.1.4 Choice of fourth-generation cephalosporins (J01DE)

Consumption of fourth-generation cephalosporins was low during 2011–2014, with cefepime and cefpirome consumed in small amounts.

10.4.2 Relative consumption of agents within fluoroquinolones (J01MA)

Quinolone antibacterials comprised between 12% and 17% of consumption of J01 antibacterials during 2011–2014 (see Table 10.4). Almost all of this quinolone consumption was from the fluoroquinolone category (J01MA). The most consumed agents were ciprofloxacin and levofloxacin, with smaller amounts of ofloxacin and norfloxacin consumed (Table 10.10). Reported consumption of newer fluoroquinolones moxifloxacin, gemifloxacin and gatifloxacin was low.

Table 10.10 Relative consumption of agents within fluoroquinolones (J01MA)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Ofloxacin	0.1 (5)	0.2 (14)	0.3 (12)	0.3 (10)
Ciprofloxacin	1.3 (50)	0.7 (42)	1 (39)	1.1 (39)
Pefloxacin	<0.1	<0.1	<0.1	<0.1
Norfloxacin	0.4 (15)	<0.1	0.3 (13)	0.3 (9)
Levofloxacin	0.7 (27)	0.6 (37)	0.8 (32)	1 (38)
Moxifloxacin	<0.1	<0.1	<0.1	0.1 (5)
Gemifloxacin	–	–	–	<0.1
Gatifloxacin	<0.1	<0.1	<0.1	<0.1
Total	**2.5**	**1.7**	**2.5**	**2.8**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

10.4.3 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

The addition of clavulanic acid to amoxicillin extends the spectrum of activity of amoxicillin against beta-lactamase-producing bacteria. Amoxicillin and clavulanic acid is recommended as second-line treatment in many treatment guidelines.

Table 10.11 summarizes the relative consumption of amoxicillin and broader-spectrum amoxicillin and clavulanic acid. Amoxicillin was the more consumed agent in all years reported.

Table 10.11 Relative consumption of amoxicillin and amoxicillin and clavulanic acid

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Amoxicillin (J01CA04)	4.4 (81)	1.9 (65)	5 (71)	3.8 (70)
Amoxicillin and clavulanic acid (J01CR02)	1 (19)	1 (35)	2.1 (29)	1.6 (30)
Total	**5.4**	**2.9**	**7.1**	**5.5**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

10.5 The 10 most consumed agents

While the number of J01 antibacterial agents available is large, there is considerable evidence from ESAC-Net and other analyses that consumption tends to be concentrated in a relatively small number.

10.5.1 The 10 most consumed agents – oral formulation

Table 10.12 summarizes consumption of the oral agents that comprise the 10 most consumed in 2014. Eight agents (amoxicillin, amoxicillin and enzyme inhibitor, levofloxacin, ciprofloxacin, sulfamethoxazole and trimethoprim, azithromycin, cefuroxime and clarithromycin) account for just under 75% of consumption. The first four of these (amoxicillin, amoxicillin and enzyme inhibitor, levofloxacin and ciprofloxacin) represent around half (51%) of all oral J01 agent consumption.

Table 10.12 The 10 most consumed agents – oral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Amoxicillin	3.52	3.52	3.52	3.52	3.52	3.52	3.52	3.52	3.52	3.52
Amoxicillin and enzyme inhibitor	1.59	1.59	1.59	1.59	1.59	1.59	1.59	1.59	1.59	
Levofloxacin	1.03	1.03	1.03	1.03	1.03	1.03	1.03	1.03		
Ciprofloxacin	0.99	0.99	0.99	0.99	0.99	0.99	0.99			
Sulfamethoxazole and trimethoprim	0.98	0.98	0.98	0.98	0.98	0.98				
Azithromycin	0.94	0.94	0.94	0.94	0.94					
Cefuroxime	0.73	0.73	0.73	0.73						
Clarithromycin	0.62	0.62	0.62							
Doxycycline	0.58	0.58								
Ampicillin	0.54									
Total consumption for this group of agents	**11.52**	**10.98**	**10.40**	**9.78**	**9.06**	**8.12**	**7.14**	**6.14**	**5.11**	**3.52**
Total consumption for all oral J01 antibacterials	**13.99**	**13.99**	**13.99**	**13.99**	**13.99**	**13.99**	**13.99**	**13.99**	**13.99**	**13.99**
Proportion (%) of total consumption for oral J01 antibacterials	**82.3%**	**78.5%**	**74.3%**	**69.9%**	**64.7%**	**58.0%**	**51.0%**	**43.9%**	**36.5%**	**25.2%**

[a] DDD: daily defined dose.

10.5.2 The 10 most consumed agents – parenteral formulation

Table 10.13 summarizes consumption of the 10 most consumed parenteral agents in 2014. Six of these (ceftriaxone, cefazolin, ampicillin, amoxicillin, cefotaxime and metronidazole) account for just over 78% of consumption. The third-generation cephalosporin ceftriaxone alone accounted for almost 30% of consumption.

Table 10.13 The 10 most consumed agents – parenteral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Ceftriaxone	1.09	1.09	1.09	1.09	1.09	1.09	1.09	1.09	1.09	1.09
Cefazolin	0.69	0.69	0.69	0.69	0.69	0.69	0.69	0.69	0.69	
Ampicillin	0.47	0.47	0.47	0.47	0.47	0.47	0.47	0.47		
Amoxicillin	0.32	0.32	0.32	0.32	0.32	0.32	0.32			
Cefotaxime	0.17	0.17	0.17	0.17	0.17	0.17				
Metronidazole	0.17	0.17	0.17	0.17	0.17					
Cefuroxime	0.14	0.14	0.14	0.14						
Gentamicin	0.13	0.13	0.13							
Streptomycin	0.08	0.08								
Ciprofloxacin	0.07									
Total consumption for this group of agents	**3.34**	**3.27**	**3.19**	**3.06**	**2.92**	**2.75**	**2.57**	**2.25**	**1.78**	**1.09**
Total consumption for all parental J01 antibacterials	**3.71**	**3.71**	**3.71**	**3.71**	**3.71**	**3.71**	**3.71**	**3.71**	**3.71**	**3.71**
Proportion (%) of total consumption for parental J01 antibacterials	**90.1%**	**88.2%**	**86.0%**	**82.5%**	**78.7%**	**74.0%**	**69.3%**	**60.6%**	**47.9%**	**29.4%**

[a] DDD: daily defined dose.

10.6 Comments

Interpretation of the data presented in this chapter relies on an understanding of the national context. The analyses are based on import and local manufacturer records, and the results suggest that import and medicine supply cycles may have a substantial impact on the estimates and explain (in part) the fluctuations between years.

Consideration could be given to exploring the use of additional data sources, such as wholesaler data, to create more robust consumption estimates. A more detailed understanding of the patterns of antimicrobial consumption would identify areas for further investigation and allow development of targeted interventions to address potential problems identified in the consumption of antibacterials.

11. SERBIA

11.1 Data sources and years of data collection

Serbia provided data for each of the four years of data collection (2011–2014). The main sources were sales records of marketing authorization holders provided by the drug agency (Table 11.1).

Table 11.1 Sources of data used for consumption estimates (2011–2014)

Year	Health care sector coverage	Data type	Data source (consumption)	Population	Data source (population)
2011	Total care	Sales records of marketing authorization holders	Drug agency	7 234 099	World Bank
2012	Total care	Sales records of marketing authorization holders	Drug agency	7 199 077	World Bank
2013	Total care	Sales records of marketing authorization holders	Drug agency	7 164 132	World Bank
2014	Total care	Sales records of marketing authorization holders	Drug agency	7 130 576	World Bank

11.2 Estimates of volumes of consumption of antibacterials for systemic use (J01)

Total consumption of antibacterials for systemic use (ATC class J01) is examined by route of administration (oral and parenteral formulations) and by pharmacological subgroup.

11.2.1 Total consumption of J01 antibacterials by route of administration

The consumption of oral and parenteral (injectable) formulations of J01 antibacterials is shown in Fig. 11.1 and summarized in Table 11.2 as DDD/1000 inhabitants per day (DID).

There is evidence of an increase in total consumption of J01 antibacterials over time (26.4 DID in 2011 to 29.5 DID in 2014). Data are based on sales of registered medicines and include the supply of inpatient and outpatient institutions.

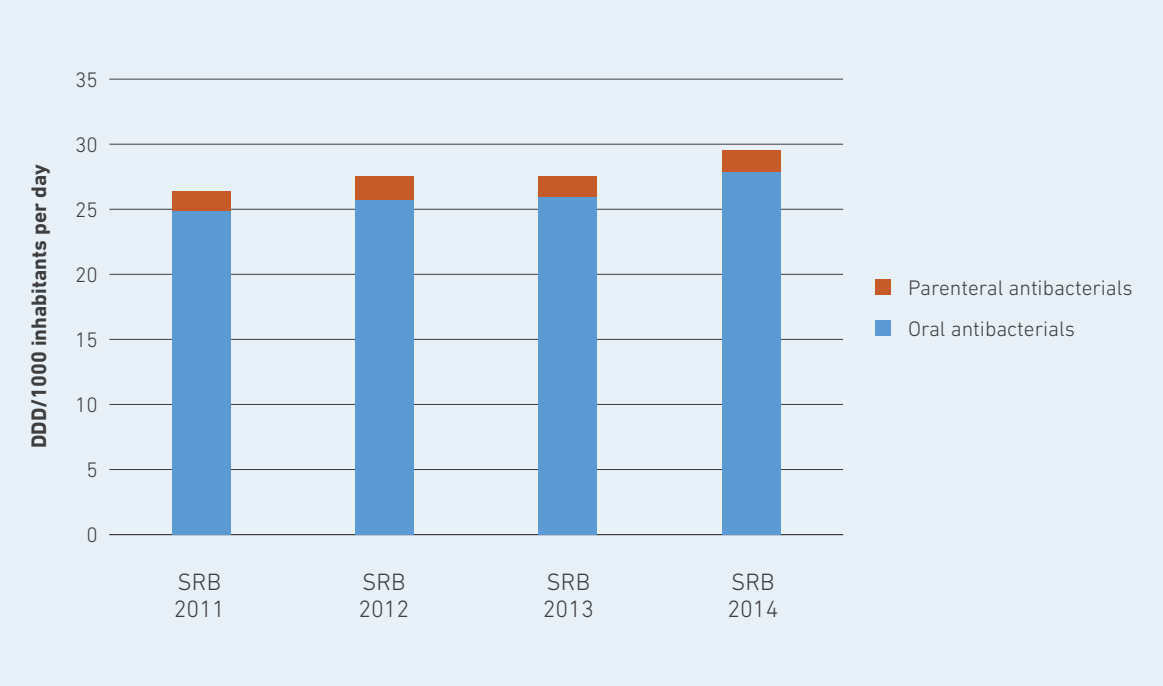

Fig. 11.1 Total consumption of J01 antibacterials by route of administration

DDD: defined daily dose.

The relative consumption of parenteral antibacterials remained reasonably stable at around 6% of total J01 consumption during the period (Table 11.2).

Table 11.2 Total consumption of J01 antibacterials by route of administration

Route of administration	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Oral J01	24.9 (94)	25.7 (93)	25.9 (94)	27.8 (94)
Parenteral J01	1.5 (6)	1.9 (7)	1.6 (6)	1.7 (6)
Total	**26.4**	**27.6**	**27.5**	**29.5**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

11.2.2 Total consumption of J01 antibacterials by pharmacological subgroup

The consumption of J01 antibacterials by pharmacological subgroup is shown in Fig. 11.2 and summarized in Table 11.3.

Numerically, the largest changes in consumption of pharmacological subgroups occurred in beta-lactams (J01C), which increased from 11.2 DID in 2011 to 13.7 DID in 2014. In addition, there is evidence of increasing consumption of cephalosporins (J01D), which increased from 3.7 DID to 4.4 DID, the sulfonamides and trimethoprim group (J01E), from 0.7 DID to 1.1 DID, and quinolones (J01M), from 2.6 DID to 3.3 DID. These were offset to some extent by reduced consumption of macrolides, lincosamides and streptogramins (J01F), which fell from 5.0 DID to 3.9 DID. Beta-lactams (J01C) showed the highest levels of consumption in 2011–2014.

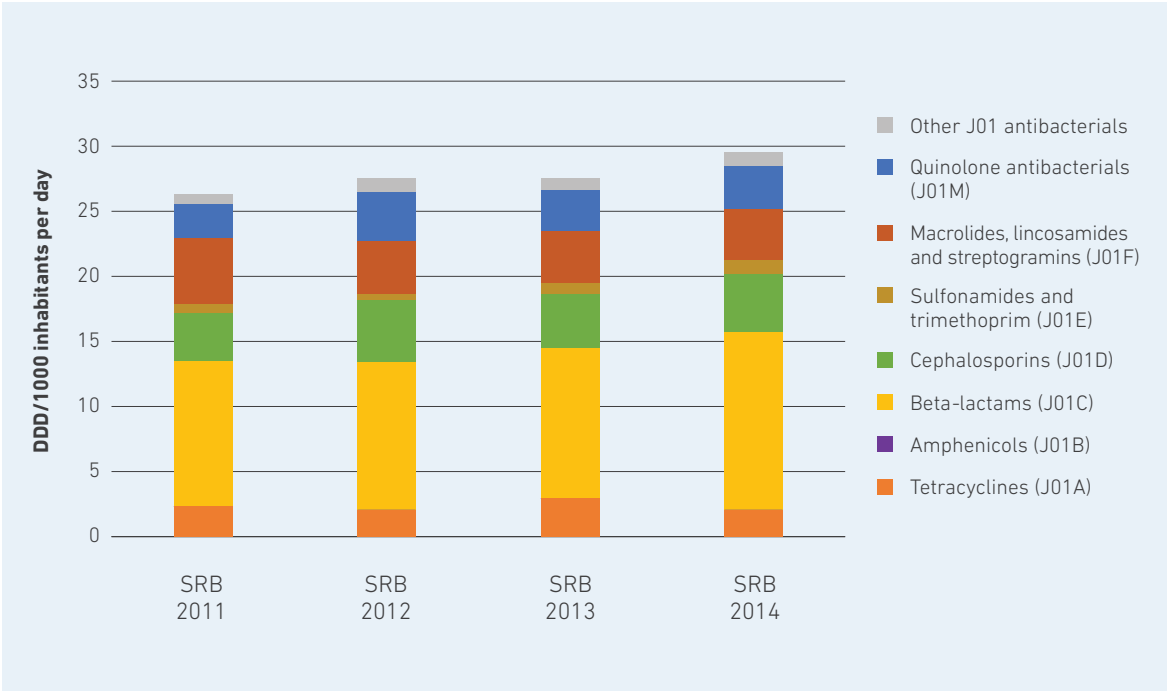

Fig. 11.2 Total consumption of J01 antibacterials by pharmacological subgroup

DDD: defined daily dose.

Table 11.3 Total consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	DDD/1000 inhabitants per day[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	2.3	2.1	2.9	2.1
Amphenicols (J01B)	<0.1	<0.1	<0.1	<0.1
Beta-lactams (J01C)	11.2	11.3	11.6	13.7
Cephalosporins (J01D)	3.7	4.7	4.1	4.4
Sulfonamides and trimethoprim (J01E)	0.7	0.5	0.9	1.1
Macrolides, lincosamides and streptogramins (J01F)	5.0	4.1	4.1	3.9
Quinolone antibacterials (J01M)	2.6	3.8	3.1	3.3
Other J01 antibacterials (J01G, J01R, J01X)	0.8	1.1	0.9	1.0
Total[b]	**26.4**	**27.6**	**27.5**	**29.5**

[a] DDD: daily defined dose. [b] Total amounts may vary slightly owing to rounding.

11.3 Relative consumption of J01 antibacterials by subgroup

11.3.1 Relative consumption of J01 antibacterials by pharmacological subgroup

The relative consumption of pharmacological subgroups measured as a proportion of total J01 antibacterials is shown in Fig. 11.3 and summarized in Table 11.4.

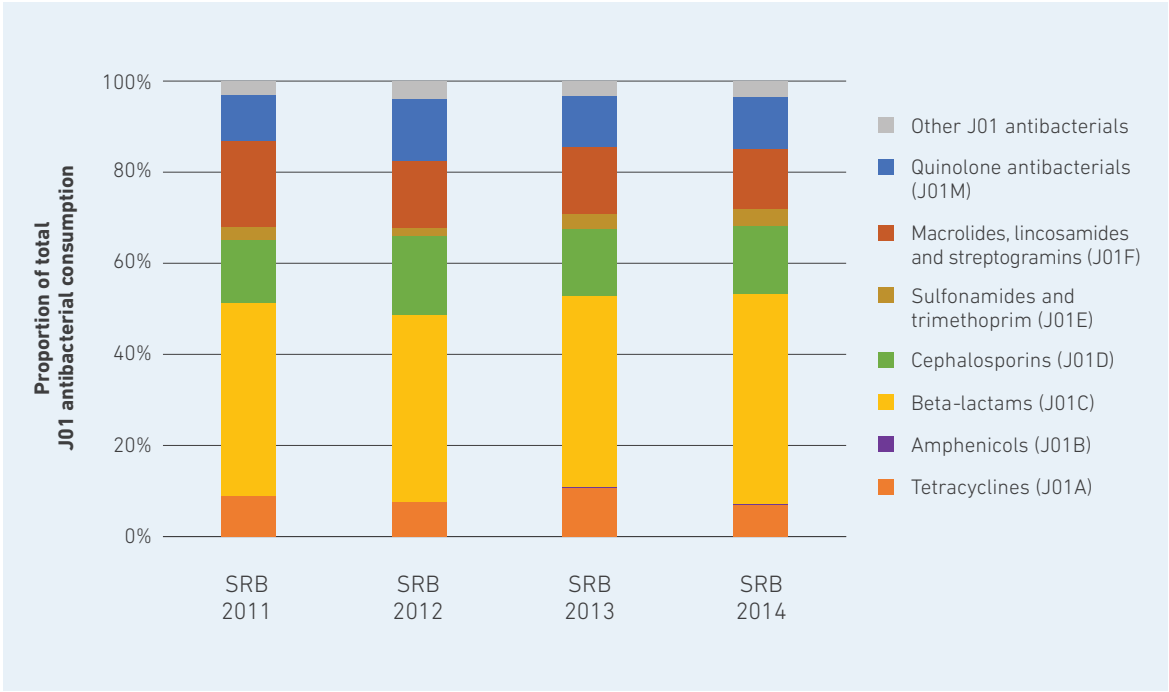

Fig. 11.3 Relative consumption of J01 antibacterials by pharmacological subgroup

Beta-lactams (J01C) was the most consumed pharmacological subgroup, at 46.2% of total consumption in 2014, followed by cephalosporins (J01D), at 14.9%, and macrolides, lincosamides and streptogramins (J01F), at 13.3%.

Consumption of the pharmacological subgroups was reasonably stable during 2011–2014, with a suggestion of increased relative consumption of beta-lactams (J01C), from 42.4% in 2011 to 46.2% in 2014, and reduced relative consumption of macrolides, lincosamides and streptogramins (J01F), from 19.1% in 2011 to 13.3% in 2014.

Table 11.4 Relative consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	Consumption as proportion of total J01 consumption (%)[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	8.8	7.5	10.7	7.0
Amphenicols (J01B)	<0.1	<0.1	<0.1	<0.1
Beta-lactams (J01C)	42.4	41.1	42.0	46.2
Cephalosporins (J01D)	14.0	17.2	14.8	14.9
Sulfonamides and trimethoprim (J01E)	2.7	1.8	3.1	3.6
Macrolides, lincosamides and streptogramins (J01F)	19.1	14.7	14.7	13.3
Quinolone antibacterials (J01M)	9.9	13.7	11.2	11.3
Other J01 antibacterials (J01G, J01R, J01X)	3.2	4.0	3.3	3.5

[a] Total percentages may vary slightly owing to rounding.

11.3.2 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Cephalosporins and quinolones are broad-spectrum antibiotics and are considered second-line antibiotics in most prescribing guidelines. Generally, it is recommended that their use should be restricted to ensure availability as second-line therapy, should first-line antibiotics fail.

The relative consumption of cephalosporins and quinolones measured as a proportion of total J01 antibacterials is shown in Fig. 11.4 and summarized in Table 11.5.

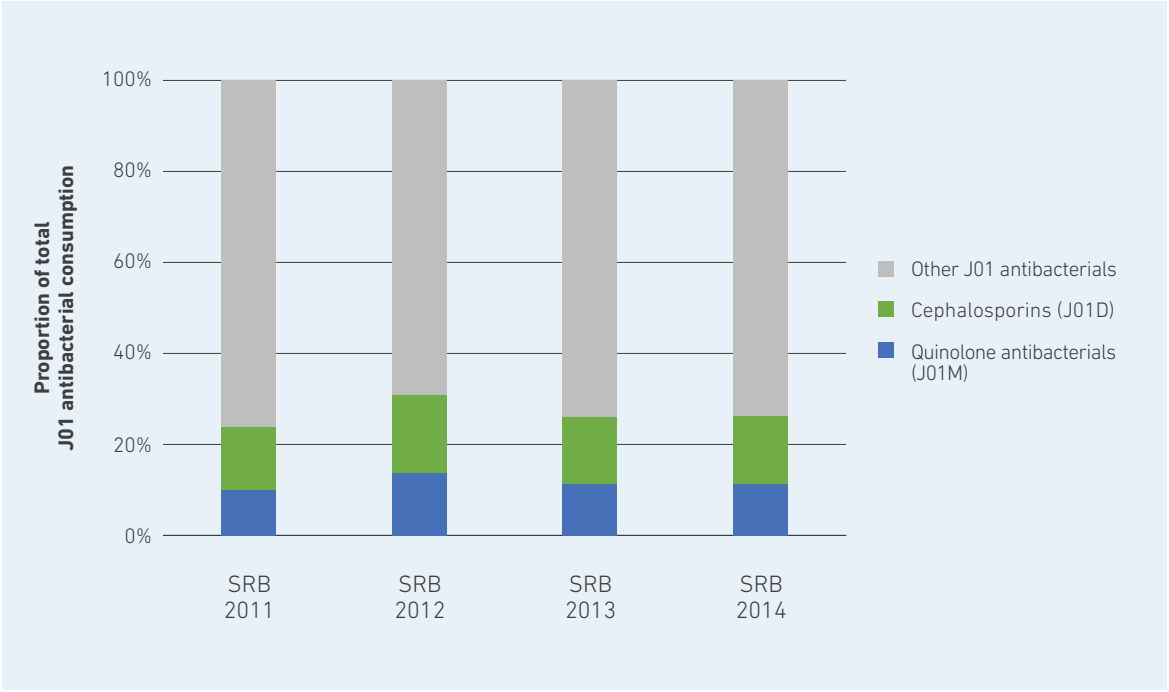

Fig. 11.4 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Consumption of quinolones and cephalosporins was reasonably stable, at around 11% and 15% respectively, in 2011–2014. Together, these two subgroups comprise around 26% of total J01 consumption in 2014 (Table 11.5).

Table 11.5 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Class of antibacterial agents	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Quinolone antibacterials (J01M)	2.6 (10)	3.8 (14)	3.1 (11)	3.3 (11)
Cephalosporins (J01D)	3.7 (14)	4.7 (17)	4.1 (15)	4.4 (15)
Other J01 antibacterials	20.1 (76)	19.1 (69)	20.4 (74)	21.8 (74)
Total	**26.4**	**27.6**	**27.5**	**29.5**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

11.4 Relative consumption by choice of agent

11.4.1 Relative consumption of cephalosporins by generation

Third- and fourth-generation cephalosporins have a broader spectrum of activity than first- and second-generation agents, with enhanced coverage of both Gram-positive and Gram-negative organisms. WHO (2012) has identified third- and fourth-generation cephalosporins as some of the agents of highest priority for risk management to ensure that critically important antimicrobials are used prudently both in human and veterinary medicine.

The relative consumption of first-, second-, third- and fourth-generation cephalosporins in 2011–2014 is shown in Fig. 11.5 and summarized in Table 11.6.

Fig. 11.5 Relative consumption of cephalosporins by generation

Most consumption was of first-generation agents (increasing from 64% in 2011 to 80% in 2014), matched by reductions in consumption of second- and third-generation cephalosporins in 2011–2014 (Table 11.6). Consumption of fourth-generation agents was very limited.

Table 11.6 Relative consumption of cephalosporins by generation

Generation	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
First-generation (J01DB)	2.3 (64)	3.5 (75)	3 (74)	3.5 (80)
Second-generation (J01DC)	0.4 (11)	0.3 (7)	0.2 (5)	0.2 (4)
Third-generation (J01DD)	0.9 (25)	0.8 (18)	0.8 (21)	0.7 (16)
Fourth-generation (J01DE)	<0.1	<0.1	<0.1	<0.1
Total	**3.6**	**4.7**	**4.0**	**4.4**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

11.4.1.1 Choice of first-generation cephalosporins (J01DB)

Table 11.7 illustrates the pattern of consumption of first-generation cephalosporins in 2011–2014. Cefalexin was the first-generation cephalosporin most consumed.

Table 11.7 Relative consumption of agents within first-generation cephalosporins (J01DB)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefalexin	2.3 (98)	3.5 (99)	2.9 (97)	3.4 (99)
Cefazolin	<0.1	<0.1	<0.1	<0.1
Cefadroxil	<0.1	<0.1	<0.1	<0.1
Total	**2.3**	**3.5**	**3.0**	**3.5**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

11.4.1.2 Choice of second-generation cephalosporins (J01DC)

Table 11.8 summarizes the pattern of consumption of second-generation cephalosporins in 2011–2014. Cefuroxime, cefaclor and cefprozil were those most consumed, although in reasonably small volumes.

Table 11.8 Relative consumption of agents within second-generation cephalosporins (J01DC)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefuroxime	0.3 (82)	0.2 (56)	0.1 (51)	<0.1
Cefaclor	<0.1	0.1 (31)	<0.1	<0.1
Cefprozil	<0.1	<0.1	<0.1	<0.1
Total	**0.4**	**0.3**	**0.2**	**0.2**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

11.4.1.3 Choice of third-generation cephalosporins (J01DD)

Table 11.9 summarizes the pattern of consumption of third-generation cephalosporins in 2011–2014. Ceftriaxone and cefixime were those most consumed.

Table 11.9 Relative consumption of agents within third-generation cephalosporins (J01DD)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefotaxime	<0.1	<0.1	<0.1	<0.1
Ceftazidime	<0.1	<0.1	<0.1	<0.1
Ceftriaxone	0.3 (34)	0.3 (38)	0.3 (38)	0.4 (61)
Cefixime	0.5 (59)	0.5 (54)	0.4 (49)	0.2 (22)
Cefoperazone	<0.1	<0.1	<0.1	<0.1
Cefpodoxime	<0.1	<0.1	<0.1	<0.1
Ceftibuten	<0.1	<0.1	<0.1	<0.1
Total	**0.9**	**0.8**	**0.8**	**0.7**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

11.4.1.4 Choice of fourth-generation cephalosporins (J01DE)

Consumption of any of the fourth-generation cephalosporins was very limited.

11.4.2 Relative consumption of agents within fluoroquinolones (J01MA)

Quinolone antibacterials comprised around 11% of consumption of J01 antibacterials during 2013–2014 (see Table 11.4). Around 74% of quinolone consumption was from fluoroquinolone category (J01MA). The most consumed agents were ciprofloxacin, levofloxacin and norfloxacin (Table 11.10).

There was some consumption of agents within the "other quinolones" category (J01MB) – namely pipemidic acid, an analogue of nalidixic acid that can be used to treat urinary tract infections (0.9 DID in 2014).

Table 11.10 Relative consumption of agents within fluoroquinolones (J01MA)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Ofloxacin	<0.1	<0.1	<0.1	<0.1
Ciprofloxacin	1.3 (76)	1.6 (59)	1.3 (59)	1.4 (59)
Norfloxacin	0.3 (17)	0.3 (13)	0.4 (17)	0.3 (13)
Levofloxacin	<0.1	0.8 (29)	0.5 (24)	0.6 (25)
Moxifloxacin	<0.1	<0.1	<0.1	<0.1
Total	**1.7**	**2.7**	**2.2**	**2.4**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

11.4.3 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

The addition of clavulanic acid to amoxicillin extends the spectrum of activity of amoxicillin against beta-lactamase-producing bacteria. Amoxicillin and clavulanic acid is recommended as second-line treatment in many treatment guidelines.

Table 11.11 summarizes the relative consumption of amoxicillin and broader-spectrum amoxicillin and clavulanic acid. Consumption was dominated by amoxicillin (78% in 2014).

Table 11.11 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Amoxicillin (J01CA04)	6.7 (64)	7.3 (74)	8.1 (75)	9.8 (78)
Amoxicillin and clavulanic acid (J01CR02)	3.8 (36)	2.6 (26)	2.7 (25)	2.7 (22)
Total	**10.5**	**10.0**	**10.8**	**12.5**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

11.5 The 10 most consumed agents

While the number of J01 antibacterial agents available is large, there is considerable evidence from ESAC-Net and other analyses that consumption tends to be concentrated in a relatively small number.

11.5.1 The 10 most consumed agents – oral formulation

Table 11.12 summarizes consumption of the oral agents that comprise the 10 most consumed in 2014. Six agents (amoxicillin, cefalexin, amoxicillin and enzyme inhibitor, doxycycline, azithromycin and ciprofloxacin) account for just over 76% of consumption.

Table 11.12 The 10 most consumed agents – oral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Amoxicillin	9.80	9.80	9.80	9.80	9.80	9.80	9.80	9.80	9.80	9.80
Cefalexin	3.43	3.43	3.43	3.43	3.43	3.43	3.43	3.43	3.43	
Amoxicillin and enzyme inhibitor	2.73	2.73	2.73	2.73	2.73	2.73	2.73	2.73		
Doxycycline	2.05	2.05	2.05	2.05	2.05	2.05	2.05			
Azithromycin	1.79	1.79	1.79	1.79	1.79	1.79				
Ciprofloxacin	1.39	1.39	1.39	1.39	1.39					
Sulfamethoxazole and trimethoprim	1.07	1.07	1.07	1.07						
Pipemidic acid	0.91	0.91	0.91							
Ampicillin	0.83	0.83								
Clarithromycin	0.81									
Total consumption for this group of agents	**24.82**	**24.01**	**23.18**	**22.26**	**21.19**	**19.80**	**18.01**	**15.96**	**13.23**	**9.80**
Total consumption for all oral J01 antibacterials	**27.82**	**27.82**	**27.82**	**27.82**	**27.82**	**27.82**	**27.82**	**27.82**	**27.82**	**27.82**
Proportion (%) of total consumption for oral J01 antibacterials	**89.2%**	**86.3%**	**83.3%**	**80.0%**	**76.2%**	**71.2%**	**64.7%**	**57.4%**	**47.5%**	**35.2%**

[a] DDD: daily defined dose.

11.5.2 The 10 most consumed agents – parenteral formulation

Table 11.13 summarizes consumption of the 10 most consumed parenteral agents (by DID) in 2014. Five of these (gentamicin, ceftriaxone, combinations of antibacterials, metronidazole and cefuroxime) account for just over 75% of consumption.

Table 11.13 The 10 most consumed agents – parenteral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Gentamicin	0.55	0.55	0.55	0.55	0.55	0.55	0.55	0.55	0.55	0.55
Ceftriaxone	0.42	0.42	0.42	0.42	0.42	0.42	0.42	0.42	0.42	
Combinations[b]	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12		
Metronidazole	0.11	0.11	0.11	0.11	0.11	0.11	0.11			
Cefuroxime	0.09	0.09	0.09	0.09	0.09	0.09				
Amikacin	0.05	0.05	0.05	0.05	0.05					
Cefazolin	0.05	0.05	0.05	0.05						
Ciprofloxacin	0.05	0.05	0.05							
Ampicillin	0.04	0.04								
Vancomycin	0.03									
Total consumption for this group of agents	**1.50**	**1.48**	**1.44**	**1.39**	**1.34**	**1.29**	**1.20**	**1.09**	**0.97**	**0.55**
Total consumption for all parental J01 antibacterials	**1.71**	**1.71**	**1.71**	**1.71**	**1.71**	**1.71**	**1.71**	**1.71**	**1.71**	**1.71**
Proportion (%) of total consumption for parental J01 antibacterials	**88.2%**	**86.5%**	**84.5%**	**81.6%**	**78.7%**	**75.7%**	**70.6%**	**63.9%**	**56.7%**	**32.3%**

[a] DDD: daily defined dose. [b] Combinations of antibacterials are: J01CA20, J01CE30, J01EB20, J01EC20 or J01ED20.

11.6 Comments

The analyses presented in this chapter are based on sales records of marketing authorization holders. Further years of data are needed to determine whether levels of antibacterial consumption will continue to rise, as occurred in 2014.

Use of complementary data sources and additional focused studies would allow more detailed understanding of the patterns of antimicrobial consumption. This would also facilitate the development of targeted interventions to address potential problems identified.

12. TAJIKISTAN

12.1 Data sources and years of data collection

Tajikistan provided data for each of the four years of data collection (2011–2014). The main sources were import records and certification records provided by the State Surveillance Service for Pharmaceutical Activities. The data cover imported, locally produced and donated medicines (Table 12.1).

Table 12.1 Sources of data used for consumption estimates (2011–2014)

Year	Health care sector coverage	Data type	Data source (consumption)	Population	Data source (population)
2011	Total care	Import records Certification records	State Surveillance Service for Pharmaceutical Activities	7 708 500[a]	The Agency for Statistics under the President of the Republic of Tajikistan
2012	Total care	Import records Certification records	State Surveillance Service for Pharmaceutical Activities	7 900 000[a]	The Agency for Statistics under the President of the Republic of Tajikistan
2013	Total care	Import records Certification records	State Surveillance Service for Pharmaceutical Activities	7 987 413[a]	The Agency for Statistics under the President of the Republic of Tajikistan
2014	Total care	Import records Certification records	State Surveillance Service for Pharmaceutical Activities	8 161 000[a]	The Agency for Statistics under the President of the Republic of Tajikistan

[a] Population estimates include the autonomous province of Gorno-Badakhshan: 207,300 (2011, 2012), 211,200 (2013) and 206,000(2014). There are small differences in estimates of DID for 2011 in this report compared to the Lancet 2014 publication as the estimates presented here are based on total population including Gorno-Badakhshan.

12.2 Estimates of volumes of consumption of antibacterials for systemic use (J01)

Total consumption of antibacterials for systemic use (ATC class J01) is examined by route of administration (oral and parenteral formulations) and by pharmacological subgroup.

12.2.1 Total consumption of J01 antibacterials by route of administration

The consumption of oral and parenteral (injectable) formulations of J01 antibacterials is shown in Fig. 12.1 and summarized in Table 12.2 as DDD/1000 inhabitants per day (DID).

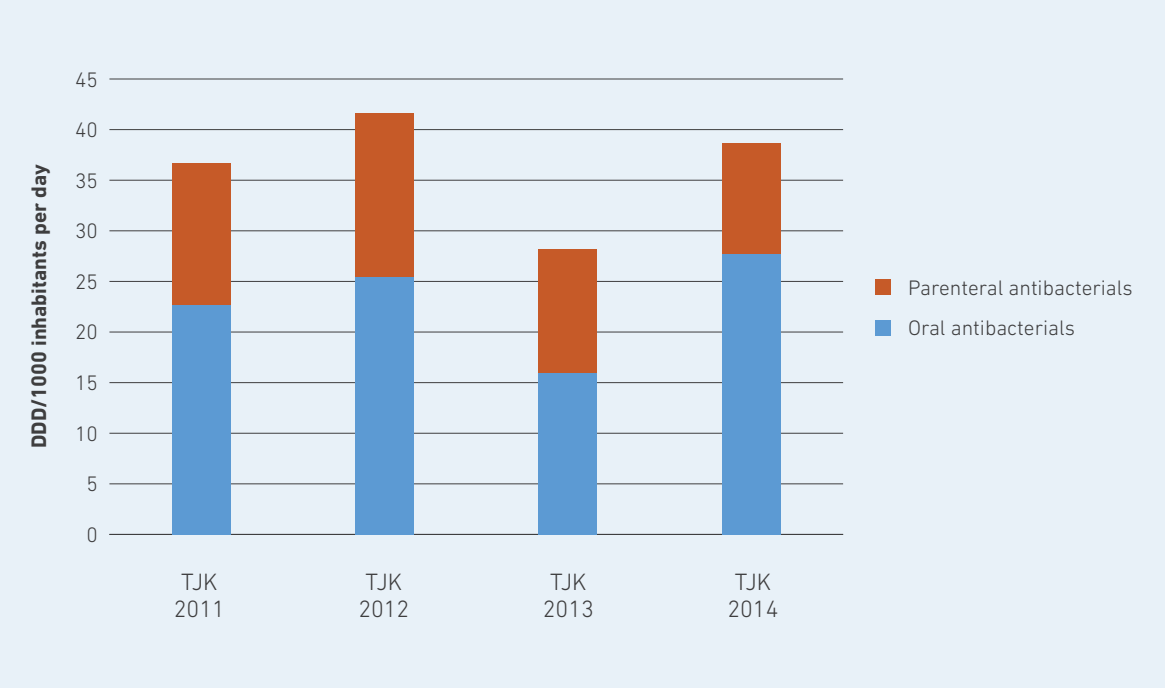

Fig. 12.1 Total consumption of J01 antibacterials by route of administration

DDD: defined daily dose.

The data indicate some fluctuations in total consumption of J01 antibacterials over time (36.6 DID in 2011 to 38.7 DID in 2014), with the highest estimate in 2012 (41.6 DID) and lowest in 2013 (28.2 DID); however, this might be explained in part by the import cycles for these medicines. The volumes of consumption of parenteral antibacterials appear to have decreased over time (14 DID in 2011 to 11 DID in 2014). Parenteral formulations constituted 28% of total J01 consumption in 2014 (Table 12.2).

Table 12.2 Total consumption of J01 antibacterials by route of administration

Route of administration	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Oral J01	22.7 (62)	25.5 (61)	15.9 (56)	27.7 (72)
Parenteral J01	14 (38)	16.1 (39)	12.3 (44)	11 (28)
Total	**36.6**	**41.6**	**28.2**	**38.7**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

12.2.2 Total consumption of J01 antibacterials by pharmacological subgroup

The consumption of J01 antibacterials by pharmacological subgroup is shown in Fig. 12.2 and summarized in Table 12.3.

Given the fluctuations in total consumption estimates it is difficult to identify clear trends in either increases or decreases of consumption of pharmacological subgroups. There appear to be increases in consumption of cephalosporins (J01D), at 5.7 DID in 2011 and 7 DID in 2014, and quinolones (J01M), at 3.5 DID in 2011 and 4 DID in 2014 (Table 12.3). The highest levels of consumption were beta-lactams (J01C), at 20.7 DID in 2014, and cephalosporins (J01D), at 7 DID in 2014.

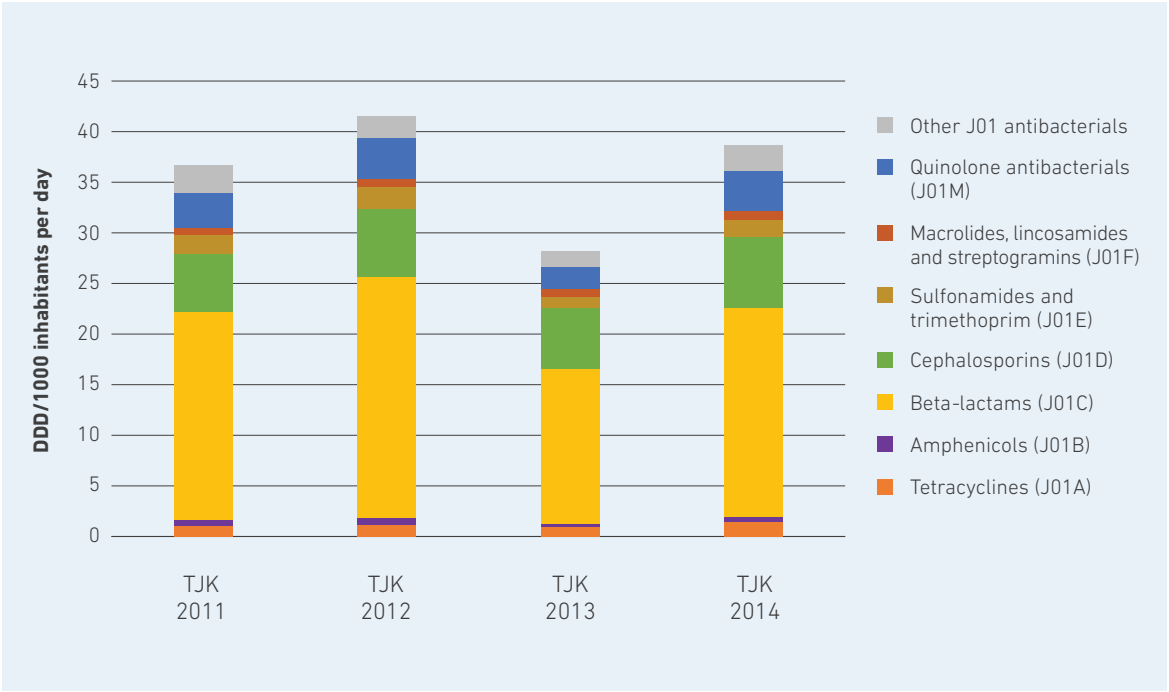

Fig. 12.2 Total consumption of J01 antibacterials by pharmacological subgroup

DDD: defined daily dose.

Table 12.3 Total consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	DDD/1000 inhabitants per day[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	1.1	1.2	0.9	1.4
Amphenicols (J01B)	0.6	0.6	0.3	0.5
Beta-lactams (J01C)	20.5	23.8	15.3	20.7
Cephalosporins (J01D)	5.7	6.7	6.1	7.0
Sulfonamides and trimethoprim (J01E)	1.9	2.2	1.1	1.7
Macrolides, lincosamides and streptogramins (J01F)	0.7	0.8	0.8	0.9
Quinolone antibacterials (J01M)	3.5	4.0	2.2	4.0
Other J01 antibacterials (J01G, J01R, J01X)	2.7	2.3	1.6	2.6
Total[b]	**36.6**	**41.6**	**28.2**	**38.7**

[a] DDD: daily defined dose. [b] Total amounts may vary slightly owing to rounding.

12.3 Relative consumption of J01 antibacterials by subgroup

12.3.1 Relative consumption of J01 antibacterials by pharmacological subgroup

The relative consumption of pharmacological subgroups measured as a proportion of total J01 antibacterials is shown in Fig. 12.3 and summarized in Table 12.4.

The data suggest small increases in relative consumption of tetracyclines (J01A), at 2.9% in 2011 and 3.7% in 2014, cephalosporins (J01D), at 15.7% in 2011 and 18.1% in 2014, and quinolones (J01M), at 9.4% in 2011 and 10.3% in 2014 (Table 12.4). Beta-lactams (J01C) was the most consumed pharmacological subgroup, at 53.5% of total J01 consumption in 2014.

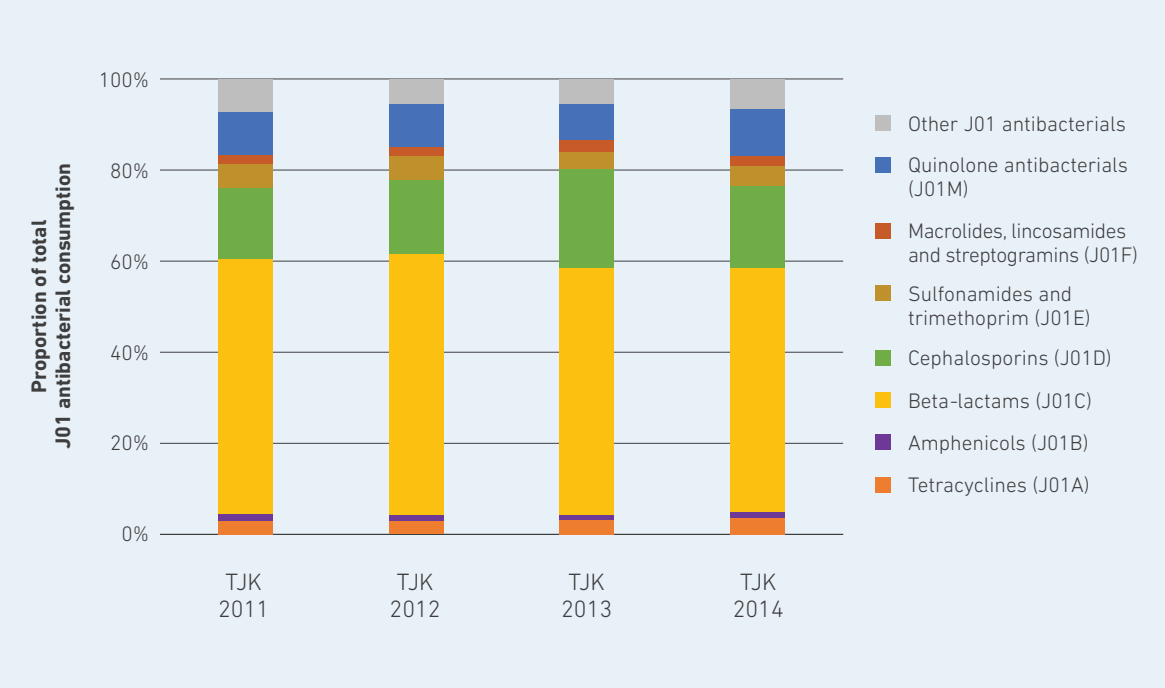

Fig. 12.3 Relative consumption of J01 antibacterials by pharmacological subgroup

Table 12.4 Relative consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	Consumption as proportion of total J01 consumption (%)[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	2.9	2.8	3.2	3.7
Amphenicols (J01B)	1.5	1.5	0.9	1.2
Beta-lactams (J01C)	56.0	57.3	54.3	53.5
Cephalosporins (J01D)	15.7	16.1	21.6	18.1
Sulfonamides and trimethoprim (J01E)	5.2	5.3	3.9	4.3
Macrolides, lincosamides and streptogramins (J01F)	2.0	2.0	2.8	2.3
Quinolone antibacterials (J01M)	9.4	9.6	7.7	10.3
Other J01 antibacterials (J01G, J01R, J01X)	7.3	5.4	5.6	6.6

[a] Total percentages may vary slightly owing to rounding.

12.3.2 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Cephalosporins and quinolones are broad-spectrum antibiotics and are considered second-line antibiotics in most prescribing guidelines. Generally, it is recommended that their use should be restricted to ensure availability as second-line therapy, should first-line antibiotics fail.

The relative consumption of cephalosporins and quinolones measured as a proportion of total J01 antibacterials is shown in Fig. 12.4 and summarized in Table 12.5. Together these two categories constitute 28% of J01 antibacterial consumption in 2014.

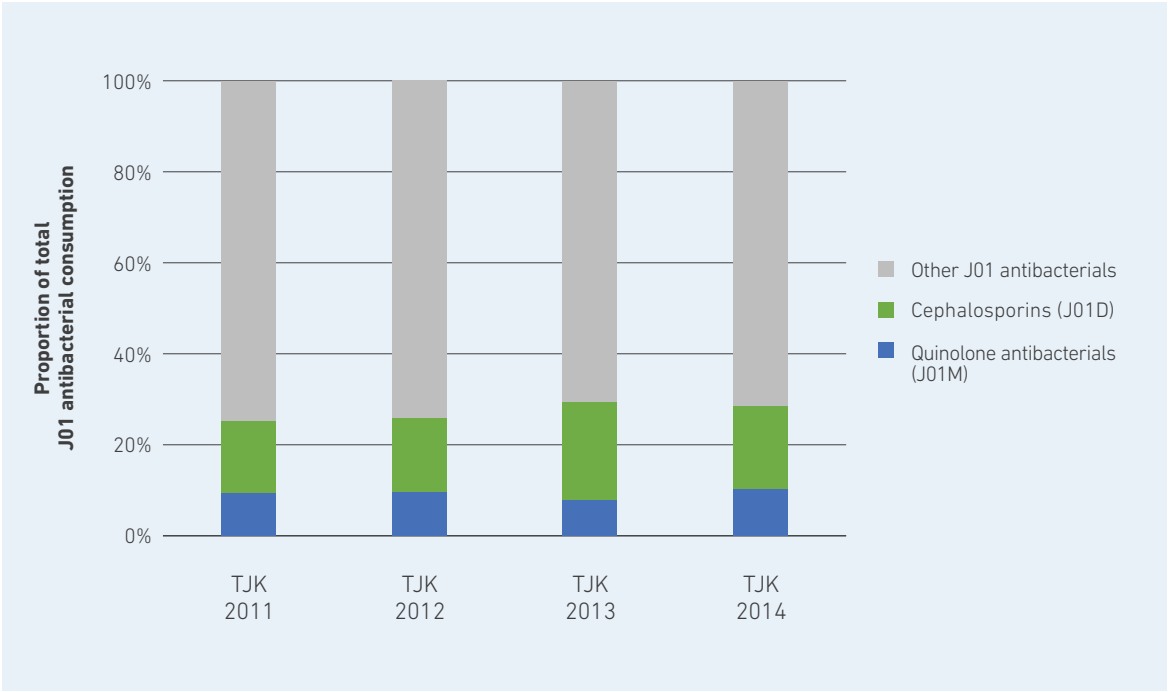

Fig. 12.4 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Table 12.5 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Class of antibacterial agents	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Quinolone antibacterials (J01M)	3.5 (9)	4 (10)	2.2 (8)	4 (10)
Cephalosporins (J01D)	5.7 (16)	6.7 (16)	6.1 (22)	7 (18)
Other J01 antibacterials	27.4 (75)	30.9 (74)	19.9 (71)	27.7 (72)
Total	**36.6**	**41.6**	**28.2**	**38.7**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

12.4 Relative consumption by choice of agent

12.4.1 Relative consumption of cephalosporins by generation

Third- and fourth-generation cephalosporins have a broader spectrum of activity than first- and second-generation agents, with enhanced coverage of both Gram-positive and Gram-negative organisms. WHO (2012) has identified third- and fourth-generation cephalosporins as some of the agents of highest priority for risk management to ensure that critically important antimicrobials are used prudently both in human and veterinary medicine.

The relative consumption of first-, second-, third- and fourth-generation cephalosporins in 2011–2014 is shown in Fig. 12.5 and summarized in Table 12.6.

Limited use of second- and fourth-generation cephalosporins was reported over time. Cephalosporin consumption was dominated by third-generation agents (83% of cephalosporin consumption in 2014; Table 12.6).

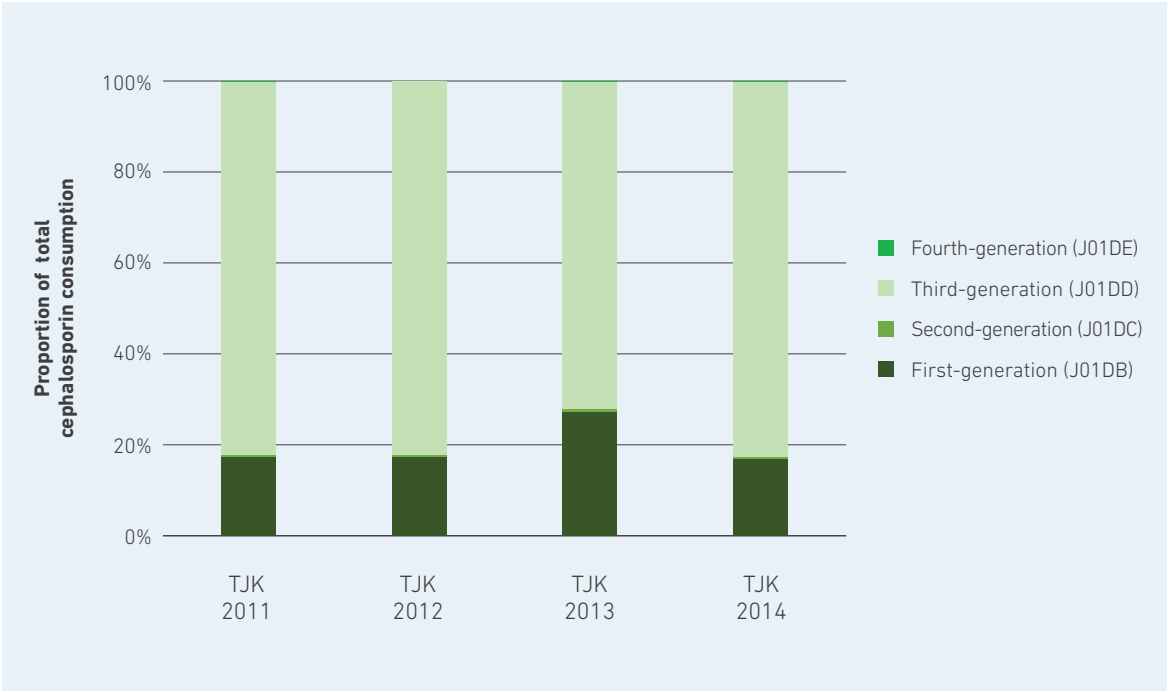

Fig. 12.5 Relative consumption of cephalosporins by generation

Table 12.6 Relative consumption of cephalosporins by generation

Generation	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
First-generation (J01DB)	1 (17)	1.2 (17)	1.7 (27)	1.2 (17)
Second-generation (J01DC)	<0.1	<0.1	<0.1	<0.1
Third-generation (J01DD)	4.7 (82)	5.5 (82)	4.4 (72)	5.8 (83)
Fourth-generation (J01DE)	<0.1	<0.1	<0.1	<0.1
Total	**5.7**	**6.7**	**6.1**	**7.0**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

12.4.1.1 Choice of first-generation cephalosporins (J01DB)

Table 12.7 illustrates the pattern of consumption of first-generation cephalosporins in 2011–2014. Consumption was dominated by cefazolin.

Table 12.7 Relative consumption of agents within first-generation cephalosporins (J01DB)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefalexin	<0.1	<0.1	<0.1	<0.1
Cefazolin	0.9 (95)	1.1 (96)	1.6 (100)	1.1 (94)
Cefadroxil	<0.1	<0.1	<0.1	<0.1
Cefradine	<0.1	<0.1	<0.1	<0.1
Total	**1.0**	**1.2**	**1.7**	**1.2**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

12.4.1.2 Choice of second-generation cephalosporins (J01DC)

Reported consumption of second-generation cephalosporins was very limited.

12.4.1.3 Choice of third-generation cephalosporins (J01DD)

Table 12.8 summarizes the pattern of consumption of third-generation cephalosporins in 2011–2014. Consumption was dominated by ceftriaxone.

Table 12.8 Relative consumption of agents within third-generation cephalosporins (J01DD)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefotaxime	<0.1	<0.1	<0.1	<0.1
Ceftazidime	<0.1	<0.1	<0.1	<0.1
Ceftriaxone	4.6 (97)	5.4 (97)	4.1 (95)	5.5 (95)
Cefixime	<0.1	<0.1	0.2 (3)	0.2 (3)
Cefoperazone	<0.1	<0.1	<0.1	<0.1
Cefpodoxime	<0.1	<0.1	<0.1	<0.1
Cefoperazone, combinations	–	–	<0.1	<0.1
Total	**4.7**	**5.5**	**4.4**	**5.8**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

12.4.1.4 Choice of fourth-generation cephalosporins (J01DE)

Reported consumption of fourth-generation cephalosporins was very limited.

12.4.2 Relative consumption of agents within fluoroquinolones (J01MA)

Quinolone antibacterials comprised around 7–10% of consumption of J01 antibacterials during 2011–2014 (see Table 12.4). Almost all quinolone consumption was from the fluoroquinolone category (J01MA). The most consumed agents were ciprofloxacin, levofloxacin and ofloxacin (Table 12.9).

Table 12.9 Relative consumption of agents within fluoroquinolones (J01MA)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Ofloxacin	0.8 (25)	1 (25)	0.2 (10)	0.1 (4)
Ciprofloxacin	1.9 (57)	2.3 (58)	1.6 (77)	3.1 (81)
Pefloxacin	<0.1	<0.1	<0.1	<0.1
Norfloxacin	<0.1	<0.1	<0.1	<0.1
Lomefloxacin	–	–	–	<0.1
Levofloxacin	0.6 (16)	0.6 (15)	0.2 (12)	0.5 (14)
Moxifloxacin	<0.1	<0.1	<0.1	<0.1
Gatifloxacin	<0.1	<0.1	<0.1	–
Total	**3.4**	**3.9**	**2.0**	**3.9**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

12.4.3 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

The addition of clavulanic acid to amoxicillin extends the spectrum of activity of amoxicillin against beta-lactamase-producing bacteria. Amoxicillin and clavulanic acid is recommended as second-line treatment in many treatment guidelines.

Table 12.10 summarizes the relative consumption of amoxicillin and broader-spectrum amoxicillin and clavulanic acid. Almost all consumption was amoxicillin.

Table 12.10 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Amoxicillin (J01CA04)	10.2 (98)	11.9 (99)	7.9 (97)	14.5 (98)
Amoxicillin and clavulanic Acid (J01CR02)	0.2 (2)	0.2 (1)	0.2 (3)	0.2 (2)
Total	**10.3**	**12.1**	**8.1**	**14.7**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

12.5 The 10 most consumed agents

While the number of J01 antibacterial agents available is large, there is considerable evidence from ESAC-Net and other analyses that consumption tends to be concentrated in a relatively small number.

12.5.1 The 10 most consumed agents – oral formulation

Table 12.11 summarizes consumption of the oral agents that comprise the 10 most consumed in 2014. Four agents (amoxicillin, ciprofloxacin, ampicillin, sulfamethoxazole and trimethoprim) account for almost 75% of consumption.

12.5.2 The 10 most consumed agents – parenteral formulation

Table 12.12 summarizes consumption of the 10 most consumed parenteral agents in 2014. Ceftriaxone alone accounts for almost 50% of consumption.

Table 12.11 The 10 most consumed agents – oral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Amoxicillin	14.48	14.48	14.48	14.48	14.48	14.48	14.48	14.48	14.48	14.48
Ciprofloxacin	3.13	3.13	3.13	3.13	3.13	3.13	3.13	3.13	3.13	
Ampicillin	1.68	1.68	1.68	1.68	1.68	1.68	1.68	1.68		
Sulfamethoxazole and trimethoprim	1.42	1.42	1.42	1.42	1.42	1.42	1.42			
Phenoxymethylpenicillin	1.25	1.25	1.25	1.25	1.25	1.25				
Nitrofurantoin	1.09	1.09	1.09	1.09	1.09					
Tetracycline	0.79	0.79	0.79	0.79						
Doxycycline	0.62	0.62	0.62							
Levofloxacin	0.49	0.49								
Chloramphenicol	0.46									
Total consumption for this group of agents	**25.41**	**24.95**	**24.46**	**23.84**	**23.05**	**21.96**	**20.72**	**19.29**	**17.61**	**14.48**
Total consumption for all oral J01 antibacterials	**27.69**	**27.69**	**27.69**	**27.69**	**27.69**	**27.69**	**27.69**	**27.69**	**27.69**	**27.69**
Proportion (%) of total consumption for oral J01 antibacterials	**91.8%**	**90.1%**	**88.3%**	**86.1%**	**83.2%**	**79.3%**	**74.8%**	**69.7%**	**63.6%**	**52.3%**

[a] DDD: daily defined dose.

Table 12.12 The 10 most consumed agents – parenteral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Ceftriaxone	5.48	5.48	5.48	5.48	5.48	5.48	5.48	5.48	5.48	5.48
Ampicillin	1.32	1.32	1.32	1.32	1.32	1.32	1.32	1.32	1.32	
Cefazolin	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11		
Combinations	0.53	0.53	0.53	0.53	0.53	0.53	0.53			
Metronidazole	0.49	0.49	0.49	0.49	0.49	0.49				
Benzathine benzylpenicillin	0.46	0.46	0.46	0.46	0.46					
Combinations of penicillins	0.39	0.39	0.39	0.39						
Gentamicin	0.25	0.25	0.25							
Benzylpenicillin	0.22	0.22								
Amikacin	0.22									
Total consumption for this group of agents	**10.49**	**10.26**	**10.04**	**9.79**	**9.40**	**8.93**	**8.44**	**7.91**	**6.80**	**5.48**
Total consumption for all parental J01 antibacterials	**10.97**	**10.97**	**10.97**	**10.97**	**10.97**	**10.97**	**10.97**	**10.97**	**10.97**	**10.97**
Proportion (%) of total consumption for parental J01 antibacterials	**95.6%**	**93.6%**	**91.6%**	**89.3%**	**85.7%**	**81.5%**	**77.0%**	**72.1%**	**62.0%**	**49.9%**

[a] DDD: daily defined dose.

12.6 Comments

Interpretation of the data presented in this chapter relies on an understanding of the national context. The analyses are based on import records, and the results suggest that import cycles may have an impact on the estimates and explain (in part) the fluctuations between years.

Consideration could be given to exploring the use of additional data sources, such as wholesaler data, to create more robust consumption estimates, including disaggregation to community and hospital sectors. A more detailed understanding of the patterns of antimicrobial consumption would identify areas for further investigation and allow development of targeted interventions to address potential problems identified in the consumption of antibacterials.

13. TURKEY

13.1 Data sources and years of data collection

Turkey provided data for each of the four years of data collection (2011–2014). The main sources were IMS Health for 2011–2012 and sales records of wholesalers derived from the pharmaceutical track and trace system for 2013–2014. The data cover imported medicines and locally manufactured medicines (Table 13.1).

Wholesaler data are provided as part of the comprehensive pharmaceutical track and trace system and cover all products in the supply and distribution chain. It is therefore expected to be a complete estimate of supplies of J01 antibacterials to pharmacies (community and hospital).

Table 13.1 Sources of data used for consumption estimates (2011–2014)

Year	Health care sector coverage	Data type	Data source (consumption)	Population	Data source (population)
2011	Community (outpatient) care	ND[a]	IMS Health	74 724 269	Turkish Statistical Institute
2012	Community (outpatient) care	ND[a]	IMS Health	75 627 384	Turkish Statistical Institute
2013	Total care	Sales records of wholesalers	Track and trace system	77 667 864	Turkish Statistical Institute
2014	Total care	Sales records of wholesalers	Track and trace system	79 295 904	Turkish Statistical Institute

[a] ND: not determined.

13.2 Estimates of volumes of consumption of antibacterials for systemic use (J01)

Total consumption of antibacterials for systemic use (ATC class J01) is examined by route of administration (oral and parenteral formulations) and by pharmacological subgroup.

13.2.1 Total consumption of J01 antibacterials by route of administration

Consumption of oral and parenteral (injectable) formulations of J01 antibacterials for 2011–2012 (outpatient care) is shown in Fig. 13.1 and for 2013–2014 (total care) in Fig. 13.2; these are summarized in Tables 13.2 and 13.3 as DDD/1000 inhabitants per day (DID).

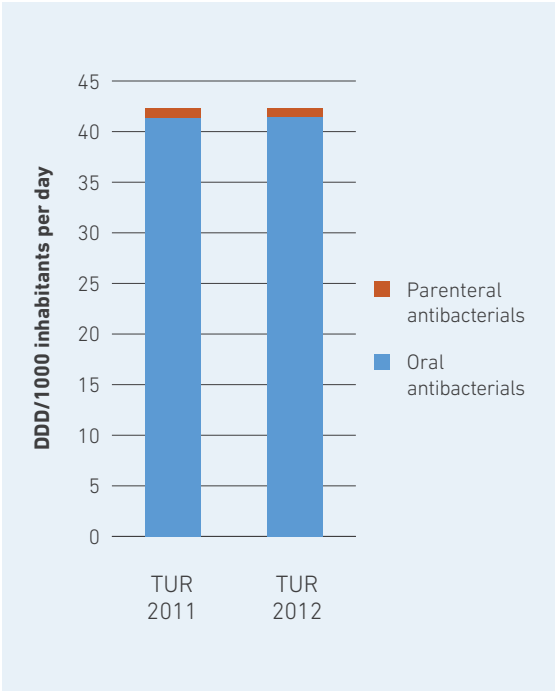

Fig. 13.1 Outpatient consumption of J01 antibacterials by route of administration (2011–2012)

DDD: defined daily dose.

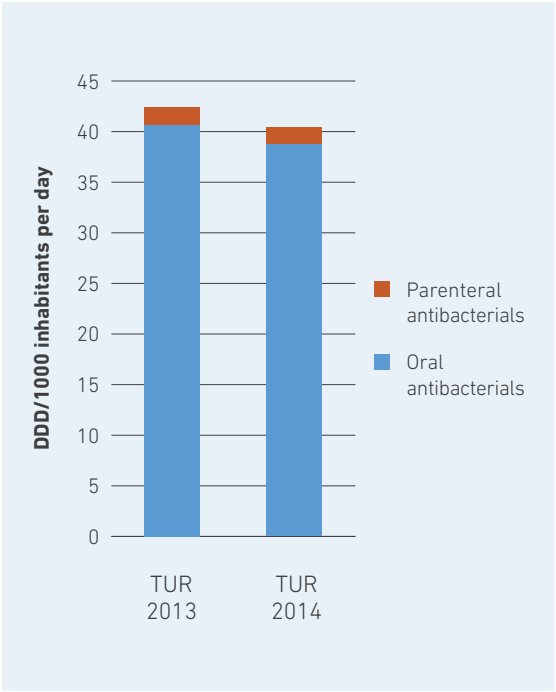

Fig. 13.2 Total consumption of J01 antibacterials by route of administration (2013–2014)

DDD: defined daily dose.

Table 13.2 Outpatient consumption of J01 antibacterials by route of administration (2011–2012)

Route of administration	DDD/1000 inhabitants per day[a] (% of total[b])	
	2011	2012
Oral J01	41.4(98)	41.4 (98)
Parenteral J01	0.9 (2)	0.9 (2)
Total	**42.3**	**42.3**

[a] DDD: daily defined dose.
[b] Total amounts and percentages may vary slightly owing to rounding.

Table 13.3 Total consumption of J01 antibacterials by route of administration (2013–2014)

Route of administration	DDD/1000 inhabitants per day[a] (% of total[b])	
	2013	2014
Oral J01	40.7(96)	38.7 (96)
Parenteral J01	1.8 (4)	1.7 (4)
Total	**42.4**	**40.4**

[a] DDD: daily defined dose.
[b] Total amounts and percentages may vary slightly owing to rounding.

The data on volume of consumption (42.3 DID) and relative consumption of parenteral formulations (2%) for outpatient care was the same for 2011 and 2012. Parenteral antibacterials comprised only 4% of total J01 consumption in 2014.

There is some indication of a reduction in total consumption of J01 antibacterials between 2013 and 2014, falling from 42.4 DID in 2013 to 40.4 in 2014. This is likely to be the result of efforts being undertaken in Turkey to reduce previously documented high levels of consumption of antibacterials.

It should be noted that population estimates of Turkish Statistical Institute are used for the calculations presented here. These estimates take account of the refugee population accommodated in Turkey (estimated at around 1 million displaced people in 2013 and 2 million in 2014). The government provides health services (including pharmaceuticals) for these displaced people.

13.2.2 Total consumption of J01 antibacterials by pharmacological subgroup

The consumption of J01 antibacterials by pharmacological subgroup in the periods 2011–2012 and 2013–2014 is shown in Figs. 13.3 and 13.4 and summarized in Tables 13.4 and 13.5.

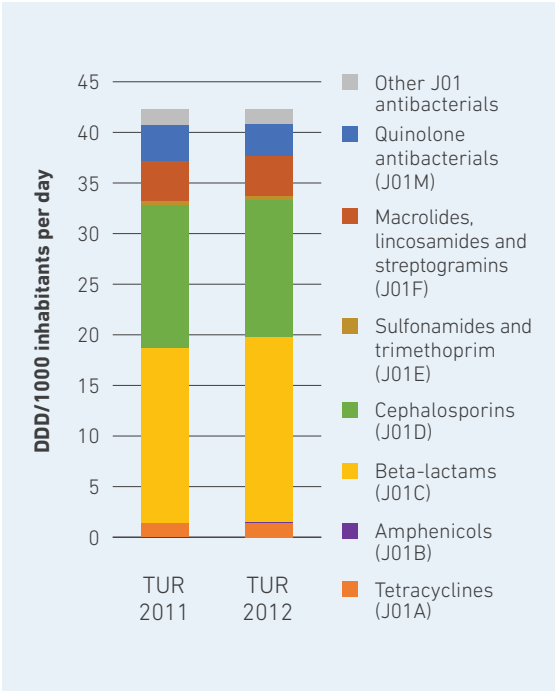

Fig. 13.3 Outpatient consumption of J01 antibacterials by pharmacological subgroup (2011–2012)

DDD: defined daily dose.

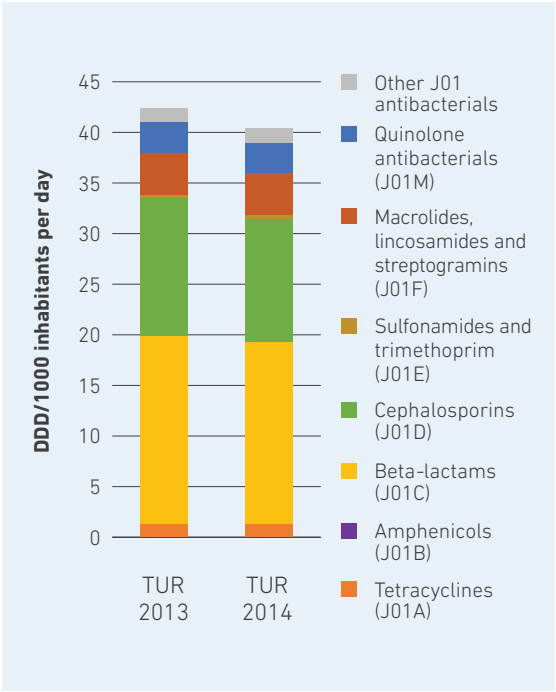

Fig. 13.4 Total consumption of J01 antibacterials by pharmacological subgroup (2013–2014)

DDD: defined daily dose.

While the volume of outpatient J01 antibacterial consumption was the same in 2011 and 2012, there were some differences among the classes of agent, with increased consumption of beta-lactams (J01C) and reduced consumption of cephalosporins (J01D) and quinolones (J01M).

The volumes of beta-lactams and cephalosporins decreased between 2013 and 2014. These form part of an overall reduction in total consumption (42.4 DID in 2013 to 40.4 DID in 2014).

Table 13.4 Outpatient consumption of J01 antibacterials by pharmacological subgroup (2011–2012)

Class of antibacterial agents	DDD/1000 inhabitants per day[a]	
	2011	2012
Tetracyclines (J01A)	1.4	1.4
Amphenicols (J01B)	<0.1	<0.1
Beta-lactams (J01C)	17.3	18.3
Cephalosporins (J01D)	14.1	13.6
Sulfonamides and trimethoprim (J01E)	0.5	0.4
Macrolides, lincosamides and streptogramins (J01F)	3.9	3.9
Quinolone antibacterials (J01M)	3.6	3.2
Other J01 antibacterials (J01G, J01R, J01X)	1.5	1.5
Total[b]	**42.3**	**42.3**

[a] DDD: daily defined dose.
[b] Total amounts may vary slightly owing to rounding.

Table 13.5 Total consumption of J01 antibacterials by pharmacological subgroup (2013–2014)

Class of antibacterial agents	DDD/1000 inhabitants per day[a]	
	2013	2014
Tetracyclines (J01A)	1.3	1.3
Amphenicols (J01B)	<0.1	<0.1
Beta-lactams (J01C)	18.6	18.0
Cephalosporins (J01D)	13.6	12.2
Sulfonamides and trimethoprim (J01E)	0.4	0.4
Macrolides, lincosamides and streptogramins (J01F)	4.1	4.1
Quinolone antibacterials (J01M)	3.1	3.0
Other J01 antibacterials (J01G, J01R, J01X)	1.4	1.5
Total[b]	**42.4**	**40.4**

[a] DDD: daily defined dose.
[b] Total amounts may vary slightly owing to rounding.

13.3 Relative consumption of J01 antibacterials by subgroup

13.3.1 Relative consumption of J01 antibacterials by pharmacological subgroup

The relative consumption of pharmacological subgroups measured as a proportion of total J01 antibacterials for outpatients in 2011–2012 and for total care in 2013–2014 are shown in Figs. 13.5 and 13.6 and summarized in Tables 13.6 and 13.7.

The relative consumption of the subgroups in outpatient care mirrors the changes in volumes, with increases in consumption of beta-lactams (J01C) and reductions in consumption of cephalosporins (J01D).

For total care (inpatient and outpatient), the relative consumption of beta-lactams was reasonably stable in 2013 and 2014 (at 44% and 44.5% respectively), with reductions in consumption of cephalosporins (32% and 30.3%) and small increases in consumption of macrolides, lincosamides and streptogramins (9.6% and 10.1%).

13.3.2 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Cephalosporins and quinolones are broad-spectrum antibiotics and are considered second-line antibiotics in most prescribing guidelines. Generally, it is recommended that their use should be restricted to ensure availability as second-line therapy, should first-line antibiotics fail.

The relative consumption of cephalosporins and quinolones measured as a proportion of total J01 antibacterials for outpatients in 2011–2012 and for total care in 2013–2014 are shown in Figs. 13.7 and 13.8 and summarized in Tables 13.8 and 13.9.

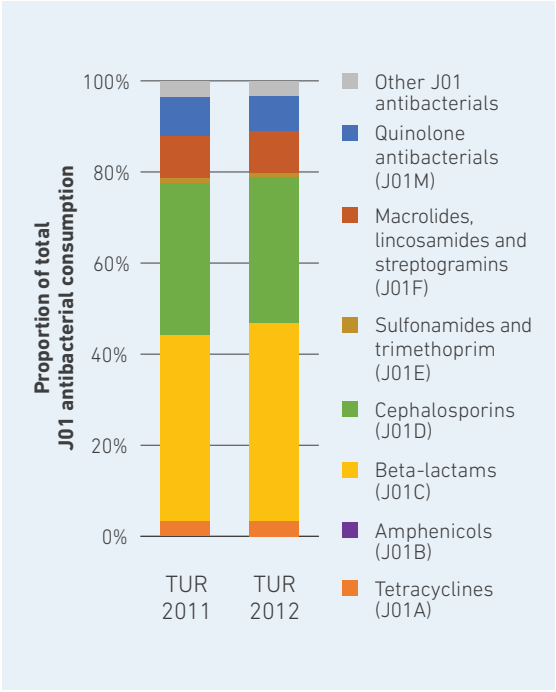

Fig. 13.5 Relative consumption of J01 antibacterials by pharmacological subgroup (2011–2012) (outpatient care)

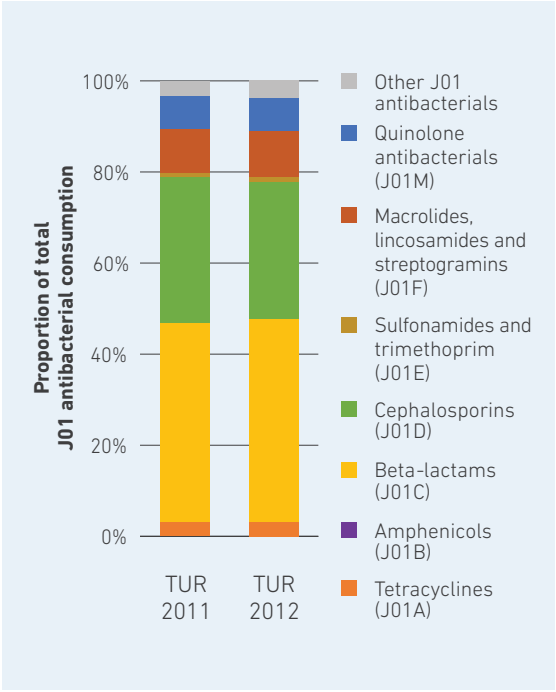

Fig. 13.6 Relative consumption of J01 antibacterials by pharmacological subgroup (2013–2014) (total care)

Table 13.6 Relative consumption of J01 antibacterials by pharmacological subgroup (2011–2012) (outpatient care)

Class of antibacterial agents	Consumption as proportion of total J01 consumption (%)[a]	
	2011	2012
Tetracyclines (J01A)	3.2	3.3
Amphenicols (J01B)	<0.1	<0.1
Beta-lactams (J01C)	41.0	43.3
Cephalosporins (J01D)	33.4	32.2
Sulfonamides and trimethoprim (J01E)	1.1	0.9
Macrolides, lincosamides and streptogramins (J01F)	9.2	9.2
Quinolone antibacterials (J01M)	8.5	7.6
Other J01 antibacterials (J01G, J01R, J01X)	3.6	3.5

[a] Total percentages may vary slightly owing to rounding.

Table 13.7 Relative consumption of J01 antibacterials by pharmacological subgroup (2013–2014) (total care)

Class of antibacterial agents	Consumption as proportion of total J01 consumption (%)[a]	
	2013	2014
Tetracyclines (J01A)	3.0	3.1
Amphenicols (J01B)	<0.1	<0.1
Beta-lactams (J01C)	43.9	44.5
Cephalosporins (J01D)	32.0	30.3
Sulfonamides and trimethoprim (J01E)	0.9	0.9
Macrolides, lincosamides and streptogramins (J01F)	9.6	10.1
Quinolone antibacterials (J01M)	7.4	7.4
Other J01 antibacterials (J01G, J01R, J01X)	3.3	3.7

[a] Total percentages may vary slightly owing to rounding.

The relative consumption of the cephalosporin and quinolone subgroups in outpatient care was reasonably stable in 2011–2012. For total care, the relative consumption of quinolones was stable in 2013–2014, with some reduction in consumption of cephalosporins (32% to 30%).

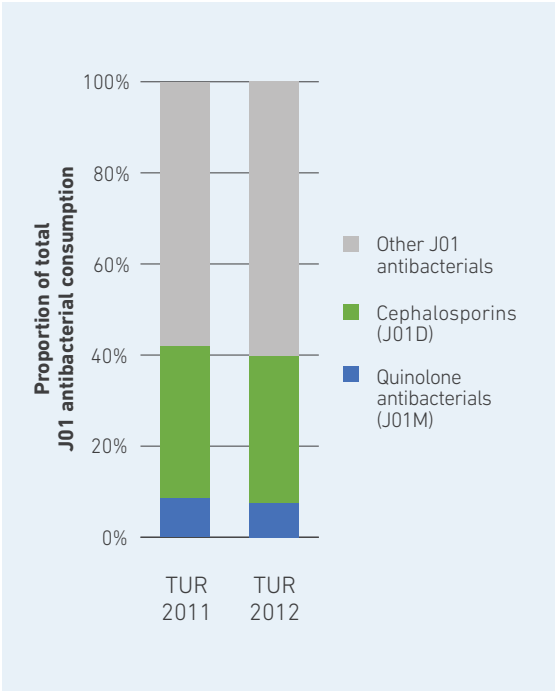

Fig. 13.7 Outpatient consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials (2011–2012)

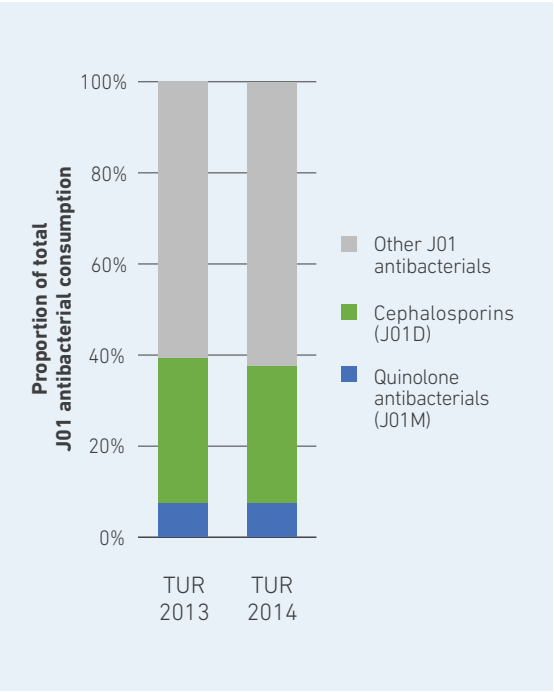

Fig. 13.8 Total consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials (2013–2014)

Table 13.8 Outpatient consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials (2011–2012)

Class of antibacterial agents	DDD/1000 inhabitants per day[a] (% of total[b])	
	2011	2012
Quinolone antibacterials (J01M)	3.6 (9)	3.2 (8)
Cephalosporins (J01D)	14.1 (33)	13.6 (32)
Other J01 antibacterials	24.6 (58)	25.5 (60)
Total	**42.3**	**42.3**

[a] DDD: daily defined dose.
[b] Total amounts and percentages may vary slightly owing to rounding.

Table 13.9 Total consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials (2013–2014)

Class of antibacterial agents	DDD/1000 inhabitants per day[a] (% of total[b])	
	2013	2014
Quinolone antibacterials (J01M)	3.1 (7)	3 (7)
Cephalosporins (J01D)	13.6 (32)	12.2 (30)
Other J01 antibacterials	25.7 (61)	25.2 (62)
Total	**42.4**	**40.4**

[a] DDD: daily defined dose.
[b] Total amounts and percentages may vary slightly owing to rounding.

13.4 Relative consumption by choice of agent

13.4.1 Relative consumption of cephalosporins by generation

Third- and fourth-generation cephalosporins have a broader spectrum of activity than first- and second-generation agents, with enhanced coverage of both Gram-positive and Gram-negative

organisms. WHO (2012) has identified third- and fourth-generation cephalosporins as some of the agents of highest priority for risk management to ensure that critically important antimicrobials are used prudently both in human and veterinary medicine.

The relative consumption of first-, second-, third- and fourth-generation cephalosporins in 2011–2012 and 2013–2014 are summarized in Tables 13.10 and 13.11.

Table 13.10 Relative consumption of cephalosporins by generation (2011–2012) (outpatient care)

Generation	DDD/1000 inhabitants per day[a] (% of total[b])	
	2011	2012
First-generation (J01DB)	0.8 (6)	0.9 (7)
Second-generation (J01DC)	9 (64)	7.5 (55)
Third-generation (J01DD)	4.2 (30)	5.2 (38)
Fourth-generation (J01DE)	<0.1	<0.1
Total	**14.1**	**13.6**

[a] DDD: daily defined dose.
[b] Total amounts and percentages may vary slightly owing to rounding.

Table 13.11 Relative consumption of cephalosporins by generation (2013–2014) (total care)

Generation	DDD/1000 inhabitants per day[a] (% of total[b])	
	2013	2014
First-generation (J01DB)	1.1 (8)	1 (8)
Second-generation (J01DC)	7.3 (54)	6.5 (54)
Third-generation (J01DD)	5.2 (38)	4.6 (38)
Fourth-generation (J01DE)	<0.1	<0.1
Total	**13.6**	**12.2**

[a] DDD: daily defined dose.
[b] Total amounts and percentages may vary slightly owing to rounding.

Consumption of fourth-generation cephalosporins was very limited (<0.1 DID) during both periods. Relative consumption patterns of first-, second- and third-generation cephalosporins were generally stable in 2013–2014.

13.4.1.1 Choice of first-generation cephalosporins (J01DB)

Tables 13.12 and 13.13 summarize the patterns of consumption of first-generation cephalosporins in 2011–2012 and 2013–2014. Cefalexin and cefazolin were those most consumed.

Table 13.12 Relative consumption of agents within first-generation cephalosporins (J01DB) (2011–2012) (outpatient care)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])	
	2011	2012
Cefalexin	0.6 (73)	0.7 (76)
Cefazolin	0.2 (27)	0.2 (24)
Cefadroxil	<0.1	<0.1
Total	**0.8**	**0.9**

[a] DDD: daily defined dose.
[b] Total amounts and percentages may vary slightly owing to rounding.

Table 13.13 Relative consumption of agents within first-generation cephalosporins (J01DB) (2013–2014) (total care)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])	
	2013	2014
Cefalexin	0.7 (68)	0.7 (69)
Cefazolin	0.3 (32)	0.3 (31)
Cefadroxil	<0.1	-
Total	**1.1**	**1.0**

[a] DDD: daily defined dose.
[b] Total amounts and percentages may vary slightly owing to rounding.

13.4.1.2 Choice of second-generation cephalosporins (J01DC)

Tables 13.14 and 13.15 summarize the patterns of consumption of second-generation cephalosporins in 2011–2012 and 2013–2014. Cefuroxime, cefaclor and cefprozil were those most consumed.

Table 13.14 Relative consumption of agents within second-generation cephalosporins (J01DC) (2011–2012) (outpatient care)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])	
	2011	2012
Cefuroxime	6.5 (72)	5.4 (71)
Cefaclor	1.4 (15)	1 (13)
Loracarbef	<0.1	<0.1
Cefprozil	1.1 (12)	1.2 (16)
Total	**9.0**	**7.5**

[a] DDD: daily defined dose.
[b] Total amounts and percentages may vary slightly owing to rounding.

Table 13.15 Relative consumption of agents within second-generation cephalosporins (J01DC) (2013–2014) (total care)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])	
	2013	2014
Cefuroxime	5.2 (72)	4.6 (71)
Cefaclor	1 (13)	1.2 (18)
Loracarbef	<0.1	-
Cefprozil	1.1 (15)	0.7 (10)
Total	**7.3**	**6.5**

[a] DDD: daily defined dose.
[b] Total amounts and percentages may vary slightly owing to rounding.

13.4.1.3 Choice of third-generation cephalosporins (J01DD)

Tables 13.16 and 13.17 summarize the patterns of consumption of third-generation cephalosporins in 2011–2012 and 2013–2014. Levels of consumption of ceftriaxone were reasonably low across 2011–2014. Cefdinir and cefixime were the most consumed agents.

Table 13.16 Relative consumption of agents within third-generation cephalosporins (J01DD) (2011–2012) (outpatient care)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])	
	2011	2012
Cefotaxime	<0.1	<0.1
Ceftazidime	<0.1	<0.1
Ceftriaxone	0.2 (5)	0.2 (4)
Ceftizoxime	<0.1	<0.1
Cefixime	1.1 (27)	1.1 (21)
Cefoperazone	<0.1	<0.1
Cefpodoxime	1.1 (25)	1.2 (22)
Ceftibuten	0.3 (6)	0.2 (3)
Cefdinir	0.9 (21)	2 (39)
Cefditoren	0.7 (16)	0.5 (10)
Total	**4.2**	**5.2**

[a] DDD: daily defined dose.
[b] Total amounts and percentages may vary slightly owing to rounding.

Table 13.17 Relative consumption of agents within third-generation cephalosporins (J01DD) (2013–2014) (total care)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])	
	2013	2014
Cefotaxime	<0.1	<0.1
Ceftazidime	<0.1	<0.1
Ceftriaxone	0.4 (8)	0.4 (9)
Ceftizoxime	<0.1	<0.1
Cefixime	1.0 (20)	1.1 (24)
Cefoperazone	<0.1	<0.1
Cefpodoxime	0.9 (17)	0.5 (11)
Ceftibuten	0.2 (5)	0.2 (5)
Cefdinir	2.2 (42)	2.1 (45)
Cefditoren	0.5 (9)	0.3 (6)
Total	**5.2**	**4.6**

[a] DDD: daily defined dose.
[b] Total amounts and percentages may vary slightly owing to rounding.

13.4.1.4 Choice of fourth-generation cephalosporins (J01DE)

Consumption of fourth-generation cephalosporins was low in 2011–2014, with cefepime and cefpirome the agents consumed in small amounts.

13.4.2 Relative consumption of agents within fluoroquinolones (J01MA)

Quinolone antibacterials comprised around 7% of consumption of J01 antibacterials during 2013–2014 (see Table13.7). Almost all quinolone consumption was from the fluoroquinolone category (J01MA). The most consumed agent was ciprofloxacin, with lower consumption of levofloxacin and moxifloxacin (Tables 13.18 and 13.19).

Table 13.18 Relative consumption of agents within fluoroquinolones (J01MA) (2011–2012) (outpatient care)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])	
	2011	2012
Ofloxacin	<0.1	<0.1
Ciprofloxacin	2.4 (66)	2.5 (77)
Pefloxacin	<0.1	<0.1
Enoxacin	<0.1	<0.1
Norfloxacin	<0.1	<0.1
Levofloxacin	0.6 (17)	0.3 (9)
Moxifloxacin	0.4 (12)	0.3 (9)
Gemifloxacin	0.1 (3)	<0.1
Total	**3.6**	**3.2**

[a] DDD: daily defined dose.
[b] Total amounts and percentages may vary slightly owing to rounding.

Table 13.19 Relative consumption of agents within fluoroquinolones (J01MA) (2013–2014) (total care)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])	
	2013	2014
Ofloxacin	<0.1	<0.1
Ciprofloxacin	2.3 (73)	2.2 (75)
Pefloxacin	<0.1	-
Enoxacin	<0.1	-
Norfloxacin	<0.1	-
Levofloxacin	0.4(12)	0.3 (11)
Moxifloxacin	0.3 (11)	0.4 (12)
Gemifloxacin	<0.1	<0.1
Total	**3.1**	**3.0**

[a] DDD: daily defined dose.
[b] Total amounts and percentages may vary slightly owing to rounding.

13.4.3 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

The addition of clavulanic acid to amoxicillin extends the spectrum of activity of amoxicillin against beta-lactamase-producing bacteria. Amoxicillin and clavulanic acid is recommended as second-line treatment in many treatment guidelines.

Tables 13.20 and 13.21 summarize the relative consumption of amoxicillin and broader-spectrum amoxicillin and clavulanic acid in the periods 2011–2012 and 2013–2014. Consumption was dominated by amoxicillin and clavulanic acid (almost 90% of use in 2014).

Table 13.20 Relative consumption of amoxicillin, amoxicillin and clavulanic acid (2011–2012) (outpatient care)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])	
	2011	2012
Amoxicillin (J01CA04)	2.6 (17)	2.6 (15)
Amoxicillin and clavulanic acid (J01CR02)	13(83)	14.3 (85)
Total	**15.6**	**16.9**

[a] DDD: daily defined dose.
[b] Total amounts and percentages may vary slightly owing to rounding.

Table 13.21 Relative consumption of amoxicillin, amoxicillin and clavulanic acid (2013–2014) (total care)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])	
	2013	2014
Amoxicillin (J01CA04)	2.2 (13)	1.9 (11)
Amoxicillin and clavulanic acid (J01CR02)	14.9(87)	15 (89)
Total	**17.1**	**16.8**

[a] DDD: daily defined dose.
[b] Total amounts and percentages may vary slightly owing to rounding.

13.5 The 10 most consumed agents

While the number of J01 antibacterial agents available is large, there is considerable evidence from ESAC-Net and other analyses that consumption tends to be concentrated in a relatively small number.

13.5.1 The 10 most consumed agents – oral formulation

Table 13.22 summarizes consumption of the oral agents that comprise the 10 most consumed in 2014. Six agents (amoxicillin and enzyme inhibitor, cefuroxime, clarithromycin, ciprofloxacin, cefdinir and amoxicillin) account for almost 75% of consumption.

Table 13.22 The 10 most consumed agents – oral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Amoxicillin and enzyme inhibitor	14.96	14.96	14.96	14.96	14.96	14.96	14.96	14.96	14.96	14.96
Cefuroxime	4.53	4.53	4.53	4.53	4.53	4.53	4.53	4.53	4.53	
Clarithromycin	3.03	3.03	3.03	3.03	3.03	3.03	3.03	3.03		
Ciprofloxacin	2.21	2.21	2.21	2.21	2.21	2.21	2.21			
Cefdinir	2.07	2.07	2.07	2.07	2.07	2.07				
Amoxicillin	1.85	1.85	1.85	1.85	1.85					
Cefaclor	1.19	1.19	1.19	1.19						
Doxycycline	1.15	1.15	1.15							
Cefixime	1.11	1.11								
Cefalexin	0.70									
Total consumption for this group of agents	**32.82**	**32.12**	**31.01**	**29.85**	**28.66**	**26.81**	**24.73**	**22.53**	**19.50**	**14.96**
Total consumption for all oral J01 antibacterials	**38.73**	**38.73**	**38.73**	**38.73**	**38.73**	**38.73**	**38.73**	**38.73**	**38.73**	**38.73**
Proportion (%) of total consumption for oral J01 antibacterials	**84.7%**	**82.9%**	**80.1%**	**77.1%**	**74.0%**	**69.2%**	**63.9%**	**58.2%**	**50.3%**	**38.6%**

[a] DDD: daily defined dose.

13.5.2 The 10 most consumed agents – parenteral formulation

Table 13.23 summarizes consumption of the 10 most consumed parenteral agents in 2014. Seven of these (ceftriaxone, cefazolin, ampicillin and enzyme inhibitor, cefuroxime, gentamicin, meropenem and clindamycin) account for just over 76% of consumption.

Table 13.23 The 10 most consumed agents – parenteral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Ceftriaxone	0.42	0.42	0.42	0.42	0.42	0.42	0.42	0.42	0.42	0.42
Cefazolin	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	0.32	
Ampicillin and enzyme inhibitor	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28		
Cefuroxime	0.11	0.11	0.11	0.11	0.11	0.11	0.11			
Gentamicin	0.07	0.07	0.07	0.07	0.07	0.07				
Meropenem	0.06	0.06	0.06	0.06	0.06					
Clindamycin	0.04	0.04	0.04	0.04						
Lincomycin	0.04	0.04	0.04							
Levofloxacin	0.03	0.03								
Teicoplanin	0.03									
Total consumption for this group of agents	**1.40**	**1.37**	**1.34**	**1.30**	**1.26**	**1.20**	**1.13**	**1.02**	**0.74**	**0.42**
Total consumption for all parental J01 antibacterials	**1.71**	**1.71**	**1.71**	**1.71**	**1.71**	**1.71**	**1.71**	**1.71**	**1.71**	**1.71**
Proportion (%) of total consumption for parental J01 antibacterials	**81.9%**	**80.3%**	**78.4%**	**76.4%**	**73.8%**	**70.5%**	**66.2%**	**59.6%**	**43.4%**	**24.5%**

[a] DDD: daily defined dose.

13.6 Comments

After antibiotic consumption data were calculated in 2011 (these were subsequently published in Lancet Infectious Diseases (Versporten et al., 2014)), Turkey undertook a range of interrelated activities to address the high levels of consumption reported. These efforts are reflected in the data for 2013 and 2014, with reductions in total J01 antibacterial consumption.

Further years of data will confirm the apparent trends towards a reduction in overall consumption. Given the large and diverse population in Turkey, examination of regional differences in patterns of consumption would provide additional opportunities for targeted interventions to support more responsible use of antimicrobial agents.

14. UZBEKISTAN

14.1 Data sources and years of data collection

Uzbekistan provided data for each of the four years of data collection (2011–2014). The main sources were import records provided by the drug agency (Table 14.1).

Table 14.1 Sources of data used for consumption estimates (2011–2014)

Year	Health care sector coverage	Data type	Data source (consumption)	Population	Data source (population)
2011	Total care	Import records	Drug agency	29 339 400	World Bank
2012	Total care	Import records	Drug agency	29 774 500	World Bank
2013	Total care	Import records	Drug agency	30 243 200	World Bank
2014	Total care	Import records	Drug agency	30 757 700	World Bank

14.2 Estimates of volumes of consumption of antibacterials for systemic use (J01)

Total consumption of antibacterials for systemic use (ATC class J01) is examined by route of administration (oral and parenteral formulations) and by pharmacological subgroup.

14.2.1 Total consumption of J01 antibacterials by route of administration

The consumption of oral and parenteral (injectable) formulations of J01 antibacterials is shown in Fig. 14.1 and summarized in Table 14.2 as DDD/1000 inhabitants per day (DID).

Most notable is the substantial increase in consumption of J01 antibacterials over time, albeit from a low baseline of 6.4 DID in 2011. Reported reasons for this increase include an increase in the number of manufacturers producing antimicrobial agents.

The reduction in consumption of parenteral antibacterials in 2014 may relate in part to efforts by the government to promote more rational and appropriate use of medicines, including antimicrobials.

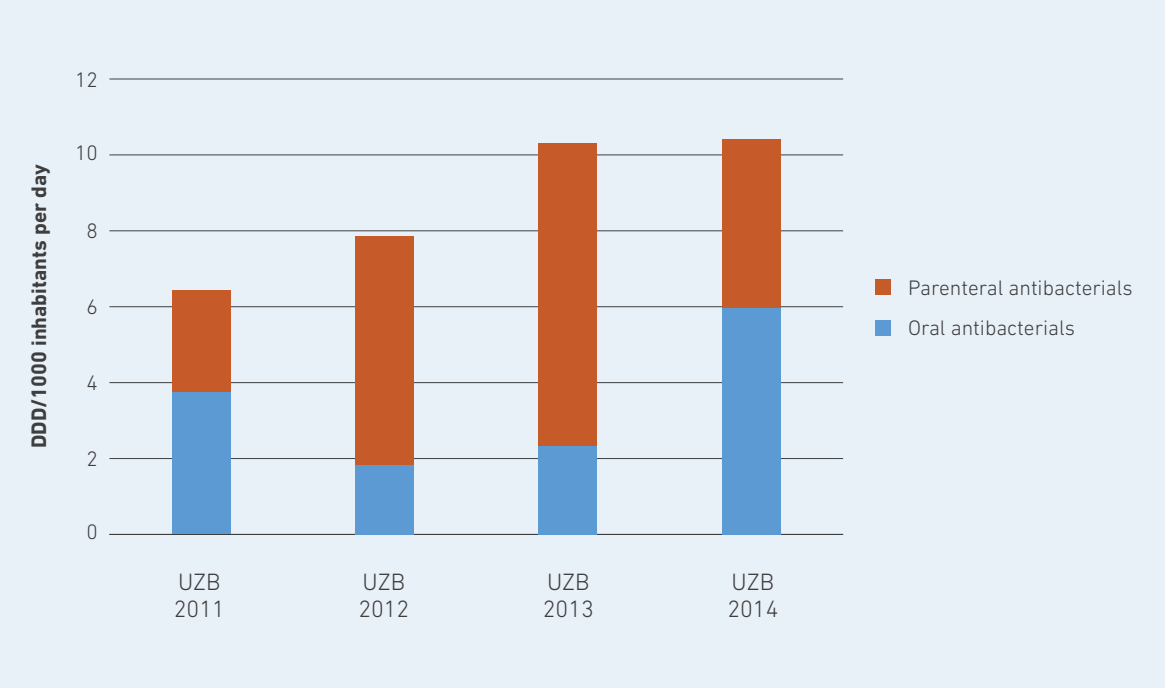

Fig. 14.1 Total consumption of J01 antibacterials by route of administration

DDD: defined daily dose.

Table 14.2 Total consumption of J01 antibacterials by route of administration

Route of administration	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Oral J01	3.7 (58)	1.8 (23)	2.3 (23)	6 (57)
Parenteral J01	2.7 (42)	6 (77)	8 (77)	4.5 (43)
Total	**6.4**	**7.9**	**10.3**	**10.4**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

14.2.2 Total consumption of J01 antibacterials by pharmacological subgroup

The consumption of J01 antibacterials by pharmacological subgroup is shown in Fig. 14.2 and summarized in Table 14.3.

It is difficult to discern trends in the consumption of the various pharmacological subgroups, given the low overall consumption of J01 antibacterials reported in 2011 and the increases in consumption in 2014. The highest levels of consumption in 2014 were beta-lactams (J01C), at 3.9 DID, and cephalosporins (J01D), at 3.1 DID. The low levels of consumption of quinolones are consistent with the low number of registered products in the J01M subgroup. Likewise, the medicines register does not include medicines in the sulfonamides and trimethoprim (J01E) class.

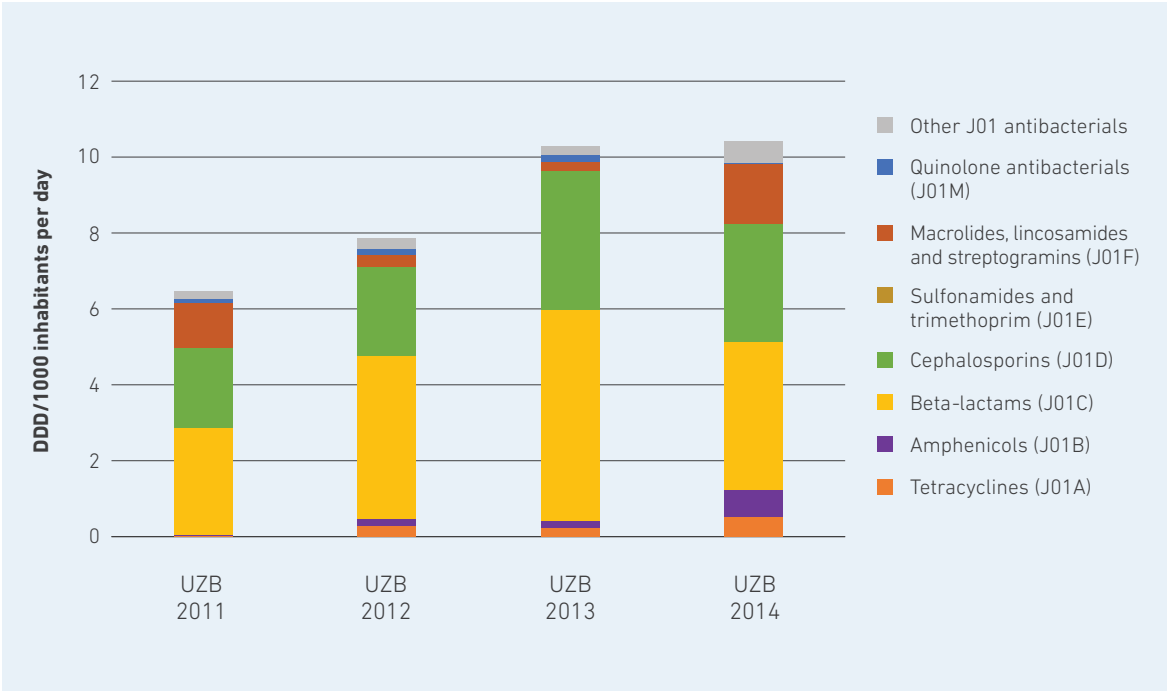

Fig. 14.2 Total consumption of J01 antibacterials by pharmacological subgroup

DDD: defined daily dose.

Table 14.3 Total consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	DDD/1000 inhabitants per day[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	0.0	0.3	0.2	0.5
Amphenicols (J01B)	0.0	0.2	0.2	0.7
Beta-lactams (J01C)	2.8	4.3	5.6	3.9
Cephalosporins (J01D)	2.1	2.4	3.7	3.1
Sulfonamides and trimethoprim (J01E)	–	–	–	–
Macrolides, lincosamides and streptogramins (J01F)	1.2	0.3	0.2	1.6
Quinolone antibacterials (J01M)	0.1	0.1	0.2	<0.1
Other J01 antibacterials (J01G, J01R, J01X)	0.2	0.3	0.3	0.6
Total[b]	**6.4**	**7.9**	**10.3**	**10.4**

[a] DDD: daily defined dose. [b] Total amounts may vary slightly owing to rounding.

14.3 Relative consumption of J01 antibacterials by subgroup

14.3.1 Relative consumption of J01 antibacterials by pharmacological subgroup

The relative consumption of pharmacological subgroups measured as a proportion of total J01 antibacterials is shown in Fig. 14.3 and summarized in Table 14.4.

While the highest levels of consumption in 2014 were beta-lactams (J01C) and cephalosporins (J01D), the relative consumption of these two groups of all J01 antibacterials decreased between 2011 and 2014. The data suggest some increases in relative consumption of tetracyclines (J01A),

from 0.3% in 2011 to 5% in 2014, and amphenicols (J01B), from 0.1% in 2011 to 6.6% in 2014, with very low levels of consumption of quinolones in 2014 (J01M), at <0.1% (Table 14.4).

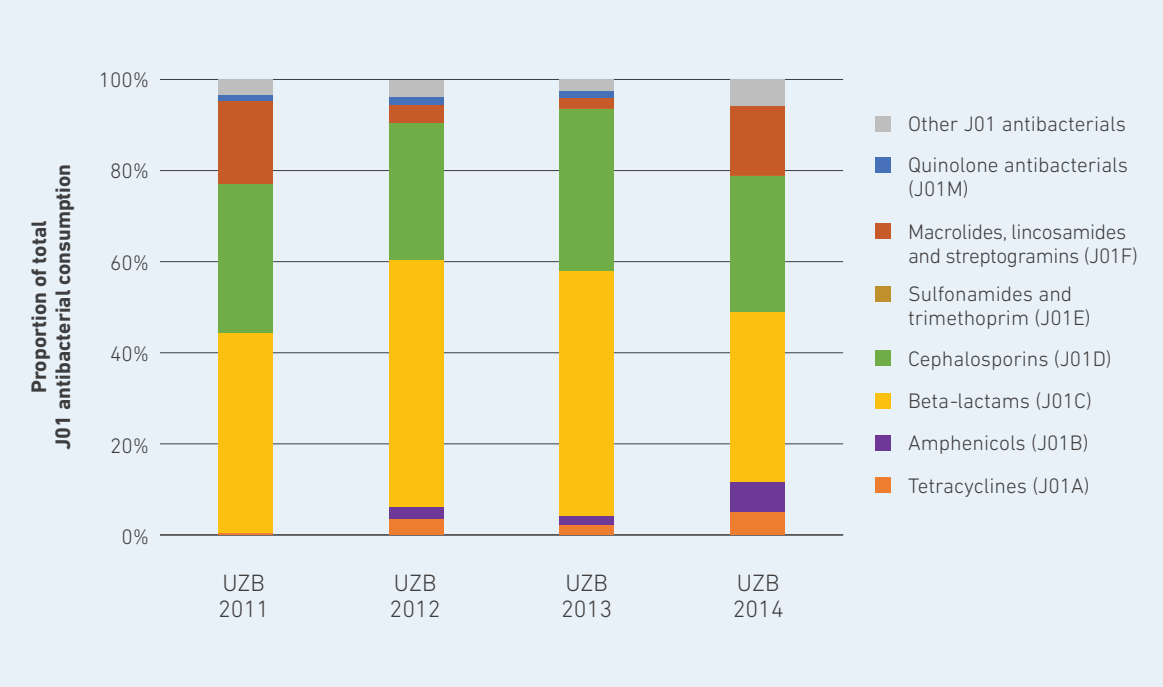

Fig. 14.3 Relative consumption of J01 antibacterials by pharmacological subgroup

Table 14.4 Relative consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	Consumption as proportion of total J01 consumption (%)[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	0.3	3.5	2.2	5.0
Amphenicols (J01B)	0.1	2.5	1.9	6.6
Beta-lactams (J01C)	43.9	54.3	54.0	37.5
Cephalosporins (J01D)	32.7	30.1	35.5	29.8
Sulfonamides and trimethoprim (J01E)	–	–	–	–
Macrolides, lincosamides and streptogramins (J01F)	18.3	3.9	2.3	15.3
Quinolone antibacterials (J01M)	1.3	1.8	1.6	<0.1
Other J01 antibacterials (J01G, J01R, J01X)	3.4	3.9	2.5	5.8

[a] Total percentages may vary slightly owing to rounding.

14.3.2 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Cephalosporins and quinolones are broad-spectrum antibiotics and are considered second-line antibiotics in most prescribing guidelines. Generally, it is recommended that their use should be restricted to ensure availability as second-line therapy, should first-line antibiotics fail.

The relative consumption of cephalosporins and quinolones measured as a proportion of total J01 antibacterials is shown in Fig. 14.4 and summarized in Table 14.5.

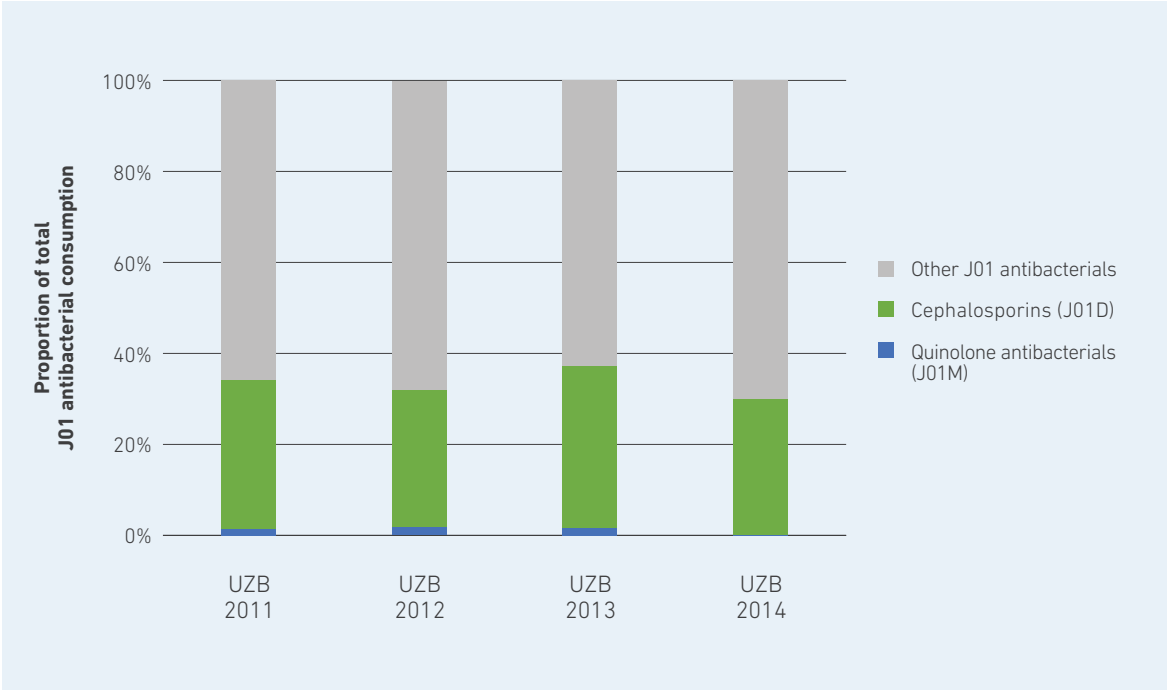

Fig. 14.4 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Relative consumption of cephalosporins was reasonably high, at 30% of total J01 consumption in 2014 (Table 14.5). By contrast, quinolone consumption was very low and was mainly consumption of ciprofloxacin and levofloxacin.

Table 14.5 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Class of antibacterial agents	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Quinolone antibacterials (J01M)	<0.1	0.1 (2)	0.2 (2)	<0.1
Cephalosporins (J01D)	2.1 (33)	2.4 (30)	3.7 (35)	3.1 (30)
Other J01 antibacterials	4.3 (66)	5.4 (68)	6.5 (63)	7.3 (70)
Total	**6.4**	**7.9**	**10.3**	**10.4**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

14.4 Relative consumption by choice of agent

14.4.1 Relative consumption of cephalosporins by generation

Third- and fourth-generation cephalosporins have a broader spectrum of activity than first- and second-generation agents, with enhanced coverage of both Gram-positive and Gram-negative organisms. WHO (2012) has identified third- and fourth-generation cephalosporins as some of the

agents of highest priority for risk management to ensure that critically important antimicrobials are used prudently both in human and veterinary medicine.

The relative consumption of first-, second-, third- and fourth-generation cephalosporins in 2011–2014 is shown in Fig. 14.5 and summarized in Table 14.6.

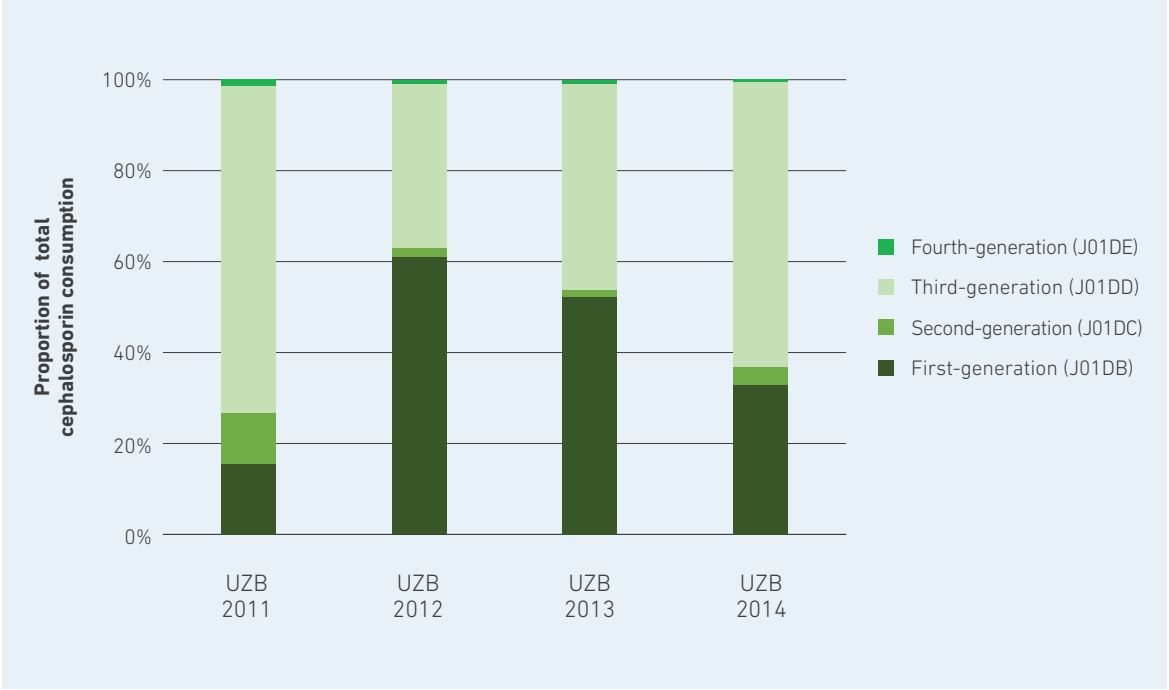

Fig. 14.5 Relative consumption of cephalosporins by generation

Use of second and fourth-generation cephalosporins over time was limited. Much cephalosporin consumption was of third-generation agents (63% of cephalosporin consumption in 2014; Table 14.6).

Table 14.6 Relative consumption of cephalosporins by generation

Generation	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
First-generation (J01DB)	0.3 (15)	1.4 (61)	1.9 (52)	1 (33)
Second-generation (J01DC)	0.2 (11)	<0.1	<0.1	0.1 (4)
Third-generation (J01DD)	1.5 (72)	0.9 (36)	1.7 (45)	1.9 (63)
Fourth-generation (J01DE)	<0.1	<0.1	<0.1	<0.1
Total	**2.1**	**2.4**	**3.7**	**3.1**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

14.4.1.1 Choice of first-generation cephalosporins (J01DB)

Table 14.7 summarizes the pattern of consumption of first-generation cephalosporins in 2011–2014. Cefazolin was the agent consumed in almost all cases.

Table 14.7 Relative consumption of agents within first-generation cephalosporins (J01DB)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefalexin	0.2 (58)	<0.1	<0.1	<0.1
Cefazolin	<0.1	1.4 (100)	1.9 (100)	1 (99)
Cefradine	<0.1	-	-	<0.1
Total	**0.3**	**1.4**	**1.9**	**1.0**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

14.4.1.2 Choice of second-generation cephalosporins (J01DC)

Consumption of second-generation cephalosporins was low; cefuroxime was the most consumed agent.

14.4.1.3 Choice of third-generation cephalosporins (J01DD)

Table 14.8 summarizes the pattern of consumption of third-generation cephalosporins in 2011–2014. Ceftriaxone was the most consumed agent.

Table 14.8 Relative consumption of agents within third-generation cephalosporins (J01DD)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefotaxime	0.5 (34)	<0.1	0.2 (15)	0.1 (6)
Ceftazidime	<0.1	<0.1	<0.1	<0.1
Ceftriaxone	0.5 (35)	0.7 (85)	1.3 (82)	1.6 (83)
Cefixime	<0.1	<0.1	<0.1	<0.1
Cefoperazone	<0.1	<0.1	<0.1	<0.1
Cefpodoxime	0.3 (24)	<0.1	<0.1	0.1 (7)
Ceftibuten	<0.1	<0.1	<0.1	<0.1
Cefoperazone, combinations	<0.1	–	–	–
Total	**1.4**	**0.8**	**1.6**	**1.9**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

14.4.1.4 Choice of fourth-generation cephalosporins (J01DE)

Levels of consumption of fourth-generation cephalosporins (cefepime and cefpirome) were low in 2011–2014.

14.4.2 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

The addition of clavulanic acid to amoxicillin extends the spectrum of activity of amoxicillin against beta-lactamase-producing bacteria. Amoxicillin and clavulanic acid is recommended as second-line treatment in many treatment guidelines.

Table 14.9 summarizes the relative consumption of amoxicillin and broader-spectrum amoxicillin and clavulanic acid. The switch in patterns of use is notable – amoxicillin and clavulanic acid dominates in 2011 (86% of consumption), but the reverse is true in 2014, with 88% of consumption

amoxicillin. The reasons for the apparent switch are not clear and require further investigation and confirmation at the country level.

Table 14.9 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Amoxicillin (J01CA04)	0.2 (14)	0.5 (92)	0.8 (94)	1.9 (88)
Amoxicillin and clavulanic acid (J01CR02)	1.2 (86)	<0.1	<0.1	0.3 (12)
Total	**1.4**	**0.5**	**0.9**	**2.2**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

14.5 The 10 most consumed agents

While the number of J01 antibacterial agents available is large, there is considerable evidence from ESAC-Net and other analyses that consumption tends to be concentrated in a relatively small number.

14.5.1 The 10 most consumed agents – oral formulation

Table 14.10 summarizes consumption of the oral agents that comprise the 10 most consumed in 2014. Five agents (amoxicillin, azithromycin, ampicillin, chloramphenicol and erythromycin) account for just over 76% of consumption.

Table 14.10 The 10 most consumed agents – oral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Amoxicillin	1.92	1.92	1.92	1.92	1.92	1.92	1.92	1.92	1.92	1.92
Azithromycin	0.86	0.86	0.86	0.86	0.86	0.86	0.86	0.86	0.86	
Ampicillin	0.71	0.71	0.71	0.71	0.71	0.71	0.71	0.71		
Chloramphenicol	0.68	0.68	0.68	0.68	0.68	0.68	0.68			
Erythromycin	0.40	0.40	0.40	0.40	0.40	0.40				
Doxycycline	0.31	0.31	0.31	0.31	0.31					
Amoxicillin and enzyme inhibitor	0.26	0.26	0.26	0.26						
Tetracycline	0.21	0.21	0.21							
Clarithromycin	0.19	0.19								
Cefpodoxime	0.14									
Total consumption for this group of agents	**5.67**	**5.53**	**5.34**	**5.13**	**4.86**	**4.56**	**4.16**	**3.48**	**2.78**	**1.92**
Total consumption for all oral J01 antibacterials	**5.96**	**5.96**	**5.96**	**5.96**	**5.96**	**5.96**	**5.96**	**5.96**	**5.96**	**5.96**
Proportion (%) of total consumption for oral J01 antibacterials	**95.1%**	**92.7%**	**89.5%**	**86.0%**	**81.6%**	**76.4%**	**69.8%**	**58.4%**	**46.6%**	**32.2%**

[a] DDD: daily defined dose.

14.5.2 The 10 most consumed agents – parenteral formulation

Table 14.11 summarizes consumption of the 10 most consumed parenteral agents in 2014. Four of these (ceftriaxone, cefazolin, ampicillin and benzylpenicillin) account for just almost 75% of consumption.

Table 14.11 The 10 most consumed agents – parenteral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Ceftriaxone	1.61	1.61	1.61	1.61	1.61	1.61	1.61	1.61	1.61	1.61
Cefazolin	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	
Ampicillin	0.47	0.47	0.47	0.47	0.47	0.47	0.47	0.47		
Benzylpenicillin	0.22	0.22	0.22	0.22	0.22	0.22	0.22			
Combinations of penicillins	0.21	0.21	0.21	0.21	0.21	0.21				
Streptomycin	0.21	0.21	0.21	0.21	0.21					
Gentamicin	0.16	0.16	0.16	0.16						
Kanamycin	0.13	0.13	0.13							
Cefotaxime	0.12	0.12								
Amikacin	0.10									
Total consumption for this group of agents	**4.24**	**4.13**	**4.01**	**3.88**	**3.72**	**3.52**	**3.30**	**3.09**	**2.62**	**1.61**
Total consumption for all parental J01 antibacterials	**4.45**	**4.45**	**4.45**	**4.45**	**4.45**	**4.45**	**4.45**	**4.45**	**4.45**	**4.45**
Proportion (%) of total consumption for parental J01 antibacterials	**95.1%**	**92.7%**	**90.1%**	**87.1%**	**83.6%**	**78.9%**	**74.1%**	**69.3%**	**58.8%**	**36.2%**

[a] DDD: daily defined dose.

14.6 Comments

The analyses presented in this chapter provide annual consumption estimates. The data indicate some considerable fluctuations in total consumption of J01 antibacterials over time, and further investigation of the sources used and completeness of data collection are needed to better understand the results.

Use of complementary data sources and additional focused studies would allow more detailed understanding of the patterns of antimicrobial consumption. This would also facilitate the development of targeted interventions to address potential problems identified.

15. KOSOVO

(in accordance with Security Council resolution 1244 (1999))

15.1 Data sources and years of data collection

Kosovo (in accordance with Security Council resolution 1244 (1999)) provided data for each of the four years of data collection (2011–2014). The main sources were import records provided by the drug agency (Table 15.1).

Table 15.1 Sources of data used for consumption estimates (2011–2014)

Year	Health care sector coverage	Data type	Data source (consumption)	Population	Data source (population)
2011	Total care	Import records	Drug agency	1 790 957	World Bank
2012	Total care	Import records	Drug agency	1 805 200	World Bank
2013	Total care	Import records	Drug agency	1 818 117	World Bank
2014	Total care	Import records	Drug agency	1 812 771	World Bank

15.2 Estimates of volumes of consumption of antibacterials for systemic use (J01)

Total consumption of antibacterials for systemic use (ATC class J01) is examined by route of administration (oral and parenteral formulations) and by pharmacological subgroup.

15.2.1 Total consumption of J01 antibacterials by route of administration

The consumption of oral and parenteral (injectable) formulations of J01 antibacterials is shown in Fig. 15.1 and summarized in Table 15.2 as DDD/1000 inhabitants per day (DID).

The data suggest a trend towards decreasing consumption of J01 antibacterials over time, although consumption estimates were higher in 2014 than in 2013. The apparent increase of consumption might be due to changes in legislation, which simplified medicines registration and import procedures, as well also allowing emergency imports, leading to more reliable data. Estimates for 2011 and 2012 may be affected by less accurate estimates of imports. Further datasets are needed to confirm trends observed in 2013–2014.

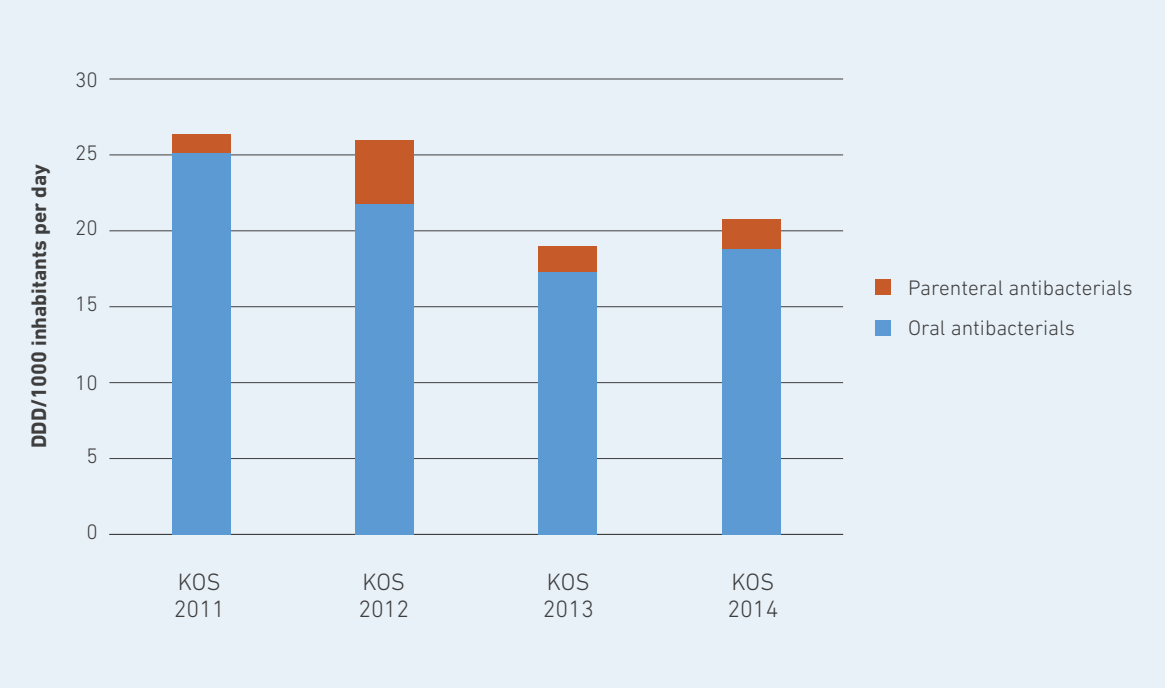

Fig. 15.1 Total consumption of J01 antibacterials by route of administration

DDD: defined daily dose.

Parenteral agents constituted 9% of total consumption of J01 antibacterials in 2013 and 2014 (Table 15.2).

Table 15.2 Total consumption of J01 antibacterials by route of administration

Route of administration	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Oral J01	25.1 (95)	21.7 (84)	17.3 (91)	18.8 (91)
Parenteral J01	1.3 (5)	4.2 (16)	1.7 (9)	2 (9)
Total	**26.4**	**26.0**	**19.0**	**20.8**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

15.2.2 Total consumption of J01 antibacterials by pharmacological subgroup

The consumption of J01 antibacterials by pharmacological subgroup is shown in Fig. 15.2 and summarized in Table 15.3.

Given the fluctuations in data, it is difficult to comment on the absolute consumption of the various pharmacological subgroups. The changes in antibacterial consumption in 2013 and 2014 may relate to the data issues noted earlier, as well as national efforts to address antimicrobial resistance, through which an intersectoral working group was created, a national strategy on antimicrobial resistance developed and an action plan adopted. Awareness campaigns were conducted for consumers and focus increased on antimicrobial resistance issues in meetings of health care professionals. These activities are likely to have contributed to the overall reductions in antibacterial consumption seen in 2013.

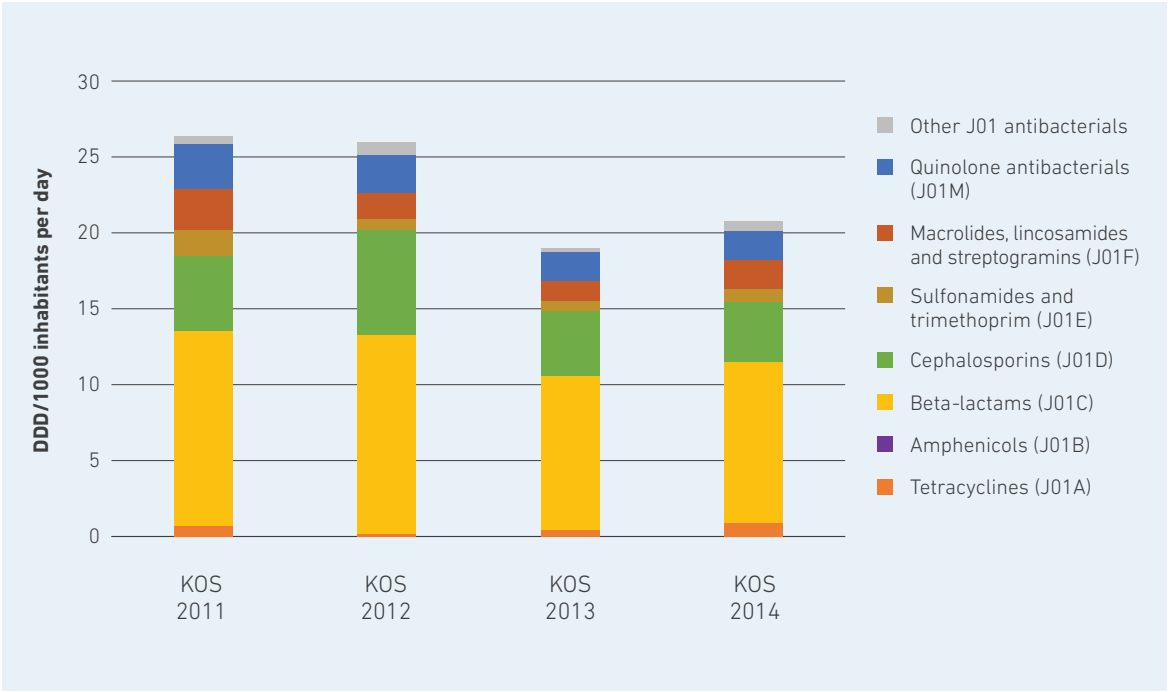

Fig. 15.2 Total consumption of J01 antibacterials by pharmacological subgroup

DDD: defined daily dose.

Table 15.3 Total consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	DDD/1000 inhabitants per day[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	0.7	0.1	0.5	0.9
Amphenicols (J01B)	–	–	–	<0.1
Beta-lactams (J01C)	12.8	13.1	10.1	10.6
Cephalosporins (J01D)	4.9	6.9	4.3	3.9
Sulfonamides and trimethoprim (J01E)	1.8	0.8	0.7	0.8
Macrolides, lincosamides and streptogramins (J01F)	2.6	1.7	1.3	1.9
Quinolone antibacterials (J01M)	3.0	2.5	1.9	1.9
Other J01 antibacterials (J01G, J01R, J01X)	0.5	0.9	0.3	0.7
Total[b]	**26.4**	**26.0**	**19.0**	**20.8**

[a] DDD: daily defined dose. [b] Total amounts may vary slightly owing to rounding.

15.3 Relative consumption of J01 antibacterials by subgroup

15.3.1 Relative consumption of J01 antibacterials by pharmacological subgroup

The relative consumption of pharmacological subgroups measured as a proportion of total J01 antibacterials is shown in Fig. 15.3 and summarized in Table 15.4.

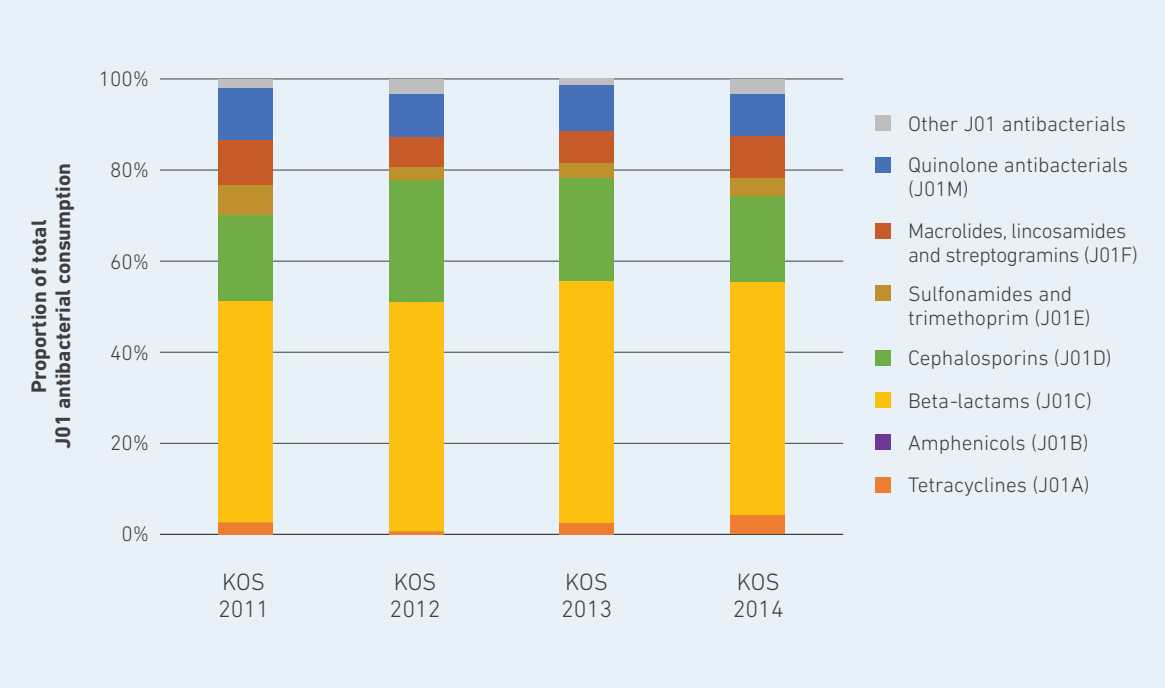

Fig. 15.3 Relative consumption of J01 antibacterials by pharmacological subgroup

The relative estimates of consumption suggest reasonably stable consumption of beta-lactams (51.2% in 2014), cephalosporins (19%) and quinolone antimicrobials (9.2%)(Table 15.4).

Table 15.4 Relative consumption of J01 antibacterials by pharmacological subgroup

Class of antibacterial agents	Consumption as proportion of total J01 consumption (%)[a]			
	2011	2012	2013	2014
Tetracyclines (J01A)	2.6	0.6	2.4	4.1
Amphenicols (J01B)	–	–	–	<0.1
Beta-lactams (J01C)	48.7	50.5	53.2	51.2
Cephalosporins (J01D)	18.7	26.6	22.5	19.0
Sulfonamides and trimethoprim (J01E)	6.7	3.0	3.5	3.9
Macrolides, lincosamides and streptogramins (J01F)	10.0	6.5	7.0	9.2
Quinolone antibacterials (J01M)	11.3	9.5	10.1	9.2
Other J01 antibacterials (J01G, J01R, J01X)	2.0	3.4	1.3	3.4

[a] Total percentages may vary slightly owing to rounding.

15.3.2 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Cephalosporins and quinolones are broad-spectrum antibiotics and are considered second-line antibiotics in most prescribing guidelines. Generally, it is recommended that their use should be restricted to ensure availability as second-line therapy, should first-line antibiotics fail.

The relative consumption of cephalosporins and quinolones measured as a proportion of total J01 antibacterials is shown in Fig. 15.4 and summarized in Table 15.5.

Relative consumption of quinolones and cephalosporins was reasonably stable over time, with the two groups combined representing around 30% of total consumption of J01 antibacterials in 2011–2014 (Table 15.5).

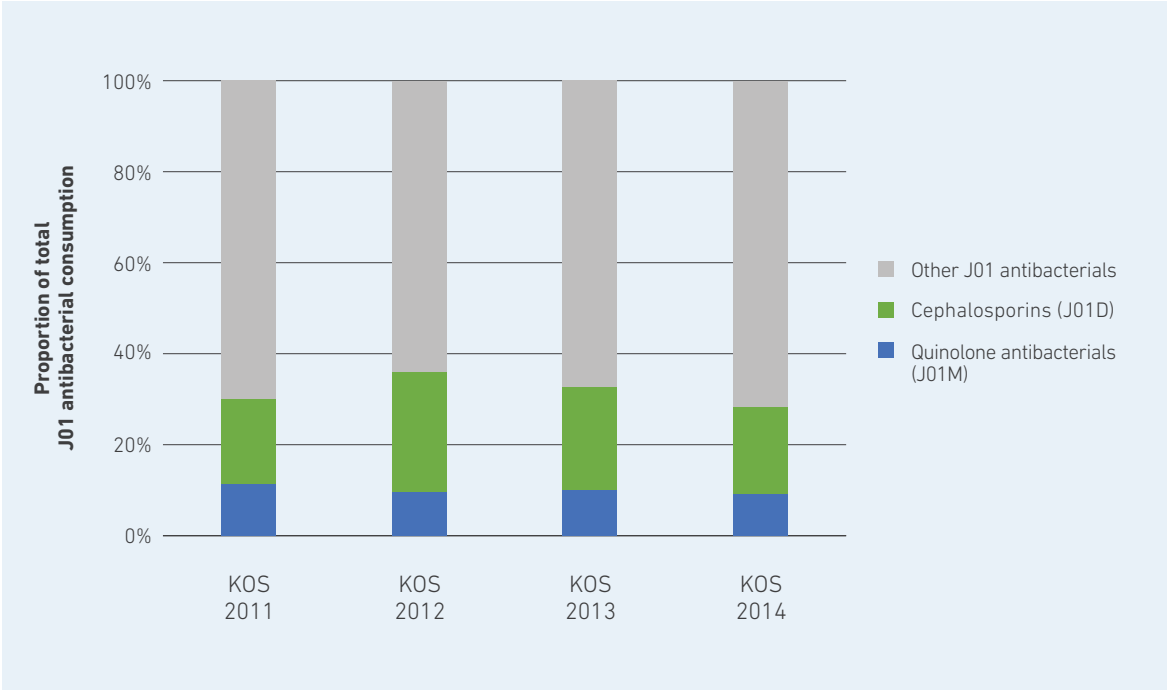

Fig. 15.4 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Table 15.5 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

Class of antibacterial agents	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Quinolone antibacterials (J01M)	3 (11)	2.5 (9)	1.9 (10)	1.9 (9)
Cephalosporins (J01D)	4.9 (19)	6.9 (27)	4.3 (23)	3.9 (19)
Other J01 antibacterials	18.5 (70)	16.6 (64)	12.8 (67)	14.9 (72)
Total	**26.4**	**26.0**	**19.0**	**20.8**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

15.4 Relative consumption by choice of agent

15.4.1 Relative consumption of cephalosporins by generation

Third- and fourth-generation cephalosporins have a broader spectrum of activity than first- and second-generation agents, with enhanced coverage of both Gram-positive and Gram-negative

organisms. WHO (2012) has identified third- and fourth-generation cephalosporins as some of the agents of highest priority for risk management to ensure that critically important antimicrobials are used prudently both in human and veterinary medicine.

The relative consumption of first-, second-, third- and fourth-generation cephalosporins in 2011–2014 is shown in Fig. 15.5 and summarized in Table 15.6.

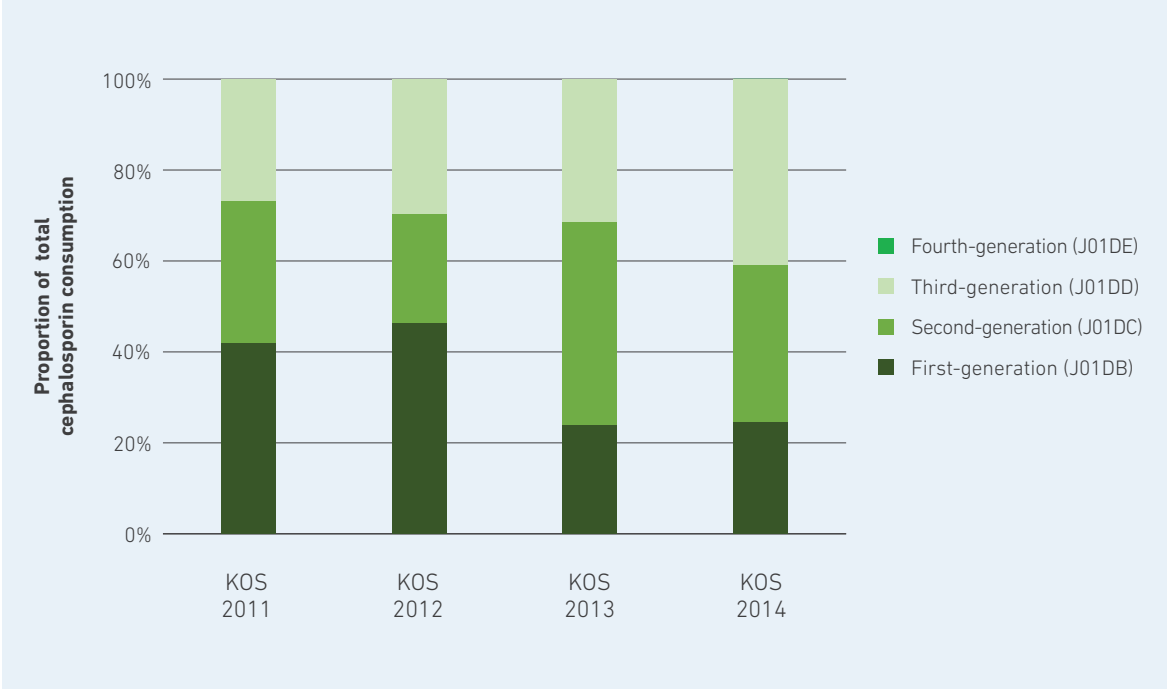

Fig. 15.5 Relative consumption of cephalosporins by generation

Very little consumption of fourth-generation agents was reported in 2011–2014. Consumption of second-generation agents fluctuated across the period and there was a trend towards increased consumption of third-generation cephalosporins (27% in 2011 and 41% in 2014; Table 15.6). Most consumption remained of first- and second-generation agents (59% in 2014).

Table 15.6 Relative consumption of cephalosporins by generation

Generation	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
First-generation (J01DB)	2.1 (42)	3.2 (46)	1 (24)	1 (25)
Second-generation (J01DC)	1.5 (31)	1.6 (24)	1.9 (45)	1.3 (34)
Third-generation (J01DD)	1.3 (27)	2.1 (30)	1.3 (31)	1.6 (41)
Fourth-generation (J01DE)	<0.1	<0.1	<0.1	-
Total	**4.9**	**6.9**	**4.3**	**3.9**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

15.4.1.1 Choice of first-generation cephalosporins (J01DB)

Table 15.7 summarizes the pattern of consumption of first-generation cephalosporins in 2011–2014. Cefalexin and cefazolin were those most consumed.

Table 15.7 Relative consumption of agents within first-generation cephalosporins (J01DB)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefalexin	2 (94)	1.3 (41)	1 (96)	0.8 (84)
Cefazolin	<0.1	1.9 (59)	<0.1	0.1 (13)
Cefadroxil	<0.1	–	–	–
Cefatrizine	–	–	<0.1	<0.1
Total	**2.1**	**3.2**	**1.0**	**1.0**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

15.4.1.2 Choice of second-generation cephalosporins (J01DC)

Table 15.8 summarizes the pattern of consumption of third-generation cephalosporins in 2011–2014. Cefuroxime and cefaclor were those most consumed.

Table 15.8 Relative consumption of agents within second-generation cephalosporins (J01DC)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefuroxime	0.1 (9)	0.6 (34)	0.6 (33)	0.5 (34)
Cefaclor	1.4 (91)	1.1 (66)	1.3 (67)	0.9 (66)
Cefprozil	–	–	–	<0.1
Total	**1.5**	**1.6**	**1.9**	**1.3**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

15.4.1.3 Choice of third-generation cephalosporins (J01DD)

Table 15.8 summarizes the pattern of consumption of third-generation cephalosporins in 2011–2014. Ceftriaxone and cefixime were the most consumed agents.

Table 15.9 Relative consumption of agents within third-generation cephalosporins (J01DD)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Cefotaxime	<0.1	<0.1	0	<0.1
Ceftazidime	<0.1	<0.1	<0.1	<0.1
Ceftriaxone	0.7 (51)	1.5 (72)	1.1 (81)	1.2 (73)
Cefixime	0.6 (49)	0.6 (28)	0.3 (19)	0.4 (25)
Cefpodoxime	-	-	<0.1	<0.1
Total	**1.3**	**2.1**	**1.3**	**1.6**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

15.4.1.4 Choice of fourth-generation cephalosporins (J01DE)

Consumption of fourth-generation cephalosporins was low during 2011–2014, with cefpirome the only agent consumed in small amounts.

15.4.2 Relative consumption of agents within fluoroquinolones (J01MA)

Quinolone antibacterials comprised around 10% of consumption of J01 antibacterials during 2011–2014 (see Table 15.4). Almost all quinolone consumption was from the fluoroquinolone category (J01MA). The most consumed agents were ciprofloxacin and levofloxacin (Table 15.10).

Table 15.10 Relative consumption of agents within fluoroquinolones (J01MA)

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Ofloxacin	<0.1	<0.1	<0.1	<0.1
Ciprofloxacin	2.6 (97)	2.1 (91)	1.3 (77)	1.3 (74)
Norfloxacin	<0.1	<0.1	<0.1	<0.1
Levofloxacin	<0.1	0.1 (6)	0.4 (22)	0.4 (23)
Moxifloxacin	<0.1	<0.1	-	<0.1
Total	**2.6**	**2.3**	**1.7**	**1.7**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

15.4.3 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

The addition of clavulanic acid to amoxicillin extends the spectrum of activity of amoxicillin against beta-lactamase-producing bacteria. Amoxicillin and clavulanic acid is recommended as second-line treatment in many treatment guidelines.

Table 15.11 summarizes the relative consumption of amoxicillin and broader-spectrum amoxicillin and clavulanic acid. The increasing consumption of amoxicillin and clavulanic acid is notable (30% relative use in 2011 increasing to 53% in 2014).

Table 15.11 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

Agent	DDD/1000 inhabitants per day[a] (% of total[b])			
	2011	2012	2013	2014
Amoxicillin (J01CA04)	6.7 (70)	7.5 (70)	5.2 (60)	4.5 (47)
Amoxicillin and clavulanic acid (J01CR02)	2.8 (30)	3.2 (30)	3.4 (40)	5 (53)
Total	**9.5**	**10.7**	**8.6**	**9.5**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

15.5 The 10 most consumed agents

While the number of J01 antibacterial agents available is large, there is considerable evidence from ESAC-Net and other analyses that consumption tends to be concentrated in a relatively small number.

15.5.1 The 10 most consumed agents – oral formulation

Table 15.12 summarizes consumption of the oral agents that comprise the 10 most consumed in 2014. Seven agents (amoxicillin and enzyme inhibitor, amoxicillin, ciprofloxacin, clarithromycin, cefaclor, sulfamethoxazole and trimethoprim and cefalexin) account for just over 76% of consumption, of which two agents (amoxicillin, amoxicillin and enzyme inhibitor) account for 50% of consumption.

Table 15.12 The 10 most consumed agents – oral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Amoxicillin and enzyme inhibitor	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00
Amoxicillin	4.48	4.48	4.48	4.48	4.48	4.48	4.48	4.48	4.48	
Ciprofloxacin	1.27	1.27	1.27	1.27	1.27	1.27	1.27	1.27		
Clarithromycin	1.15	1.15	1.15	1.15	1.15	1.15	1.15			
Cefaclor	0.89	0.89	0.89	0.89	0.89	0.89				
Sulfamethoxazole and trimethoprim	0.81	0.81	0.81	0.81	0.81					
Cefalexin	0.81	0.81	0.81	0.81						
Doxycycline	0.79	0.79	0.79							
Phenoxymethylpenicillin	0.65	0.65								
Azithromycin	0.64									
Total consumption for this group of agents	**16.48**	**15.84**	**15.19**	**14.40**	**13.60**	**12.79**	**11.90**	**10.75**	**9.48**	**5.00**
Total consumption for all oral J01 antibacterials	**18.81**	**18.81**	**18.81**	**18.81**	**18.81**	**18.81**	**18.81**	**18.81**	**18.81**	**18.81**
Proportion (%) of total consumption for oral J01 antibacterials	**87.6%**	**84.2%**	**80.8%**	**76.6%**	**72.3%**	**68.0%**	**63.3%**	**57.2%**	**50.4%**	**26.6%**

[a] DDD: daily defined dose.

15.5.2 The 10 most consumed agents – parenteral formulation

Table 15.13 summarizes consumption of the 10 most consumed parenteral agents in 2014. Just two of these (ceftriaxone and gentamicin) account for just over 81% of consumption.

Table 15.13 The 10 most consumed agents – parenteral formulation (2014)

Agent	DDD/1000 inhabitants per day[a]									
	Top 10	Top 9	Top 8	Top 7	Top 6	Top 5	Top 4	Top 3	Top 2	Top 1
Ceftriaxone	1.17	1.17	1.17	1.17	1.17	1.17	1.17	1.17	1.17	1.17
Gentamicin	0.43	0.43	0.43	0.43	0.43	0.43	0.43	0.43	0.43	
Cefazolin	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12		
Streptomycin	0.07	0.07	0.07	0.07	0.07	0.07	0.07			
Benzylpenicillin	0.04	0.04	0.04	0.04	0.04	0.04				
Imipenem and enzyme inhibitor	0.02	0.02	0.02	0.02	0.02					
Metronidazole	0.02	0.02	0.02	0.02						
Combinations	0.02	0.02	0.02							
Ciprofloxacin	0.02	0.02								
Amikacin	0.01									
Total consumption for this group of agents	**1.93**	**1.91**	**1.89**	**1.87**	**1.85**	**1.83**	**1.79**	**1.73**	**1.60**	**1.17**
Total consumption for all parental J01 antibacterials	**1.97**	**1.97**	**1.97**	**1.97**	**1.97**	**1.97**	**1.97**	**1.97**	**1.97**	**1.97**
Proportion (%) of total consumption for parental J01 antibacterials	**97.9%**	**97.1%**	**96.1%**	**95.1%**	**94.1%**	**92.8%**	**91.0%**	**87.6%**	**81.3%**	**59.4%**

[a] DDD: daily defined dose.

15.6 Comments

The analyses presented in this chapter are based on import records, and the results suggest that import cycles and data quality issues may have an impact on the estimates and explain (in part) the fluctuations between years. Further years of data are needed to determine trends in antibacterial consumption.

16. CROSS-NATIONAL COMPARISONS

16.1 Background

As the methods of data collection for ESAC-Net and WHO AMC Network are broadly similar, it is possible to combine the datasets for an extended comparison of EU and non-EU countries and areas in Europe. Cross-national comparisons using 2014 data were conducted for the key metrics used in this report.

16.2 Estimates of volumes of consumption of antibacterials for systemic use (J01)

Total consumption of antibacterials for systemic use (ATC class J01) is examined by route of administration (oral and parenteral formulations) and by pharmacological subgroup.

16.2.1 Total consumption of J01 antibacterials by route of administration

The consumption of oral and parenteral (injectable) formulations of J01 antibacterials is shown in Fig. 16.1 and summarized in Table 16.1 as DDD/1000 inhabitants per day (DID).

The results illustrate the variability between countries and areas in total consumption of J01 antibacterials in 2014. DDD/1000 inhabitants per day ranged from 40.4 DID (Turkey) to 8.5 DID (Azerbaijan). The average total consumption across the 12 datasets was 24.4 DID.

This variability was also reflected in the relative consumption of parenteral forms of J01 antibacterials – ranging from 69% (Azerbaijan) to 4% (Turkey)(Table 16.1).

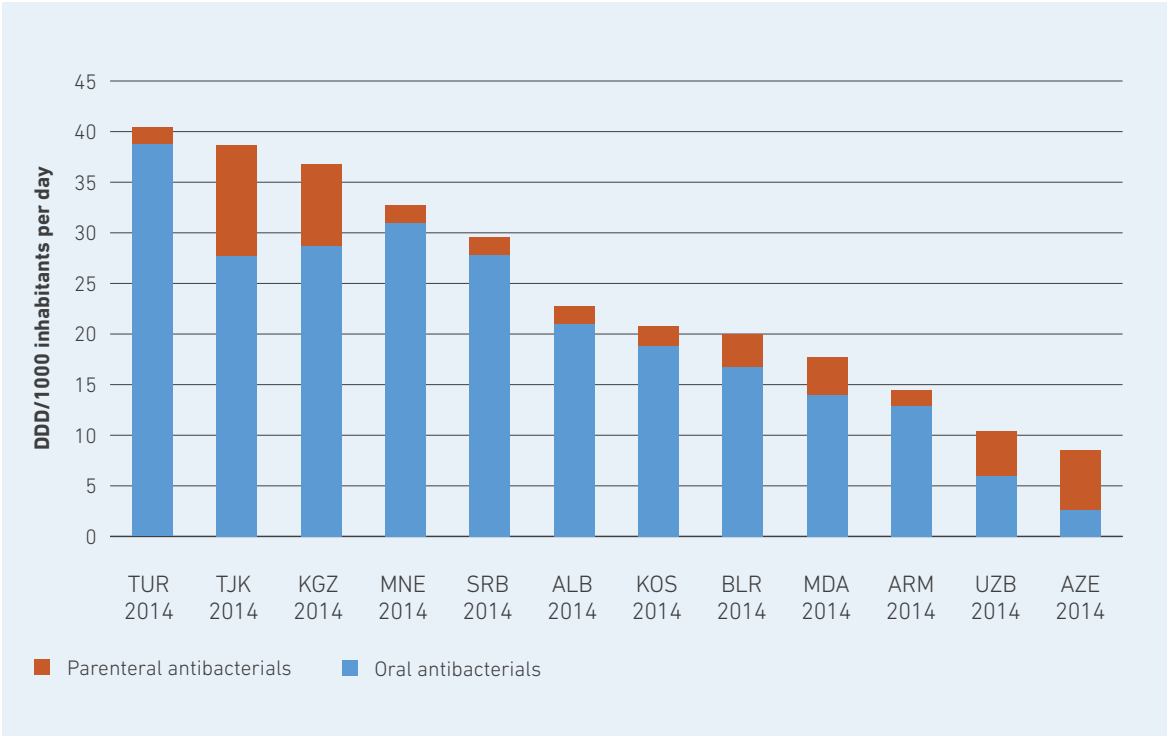

Fig. 16.1 Total consumption of J01 antibacterials by route of administration (2014)[4]

DDD: defined daily dose.

Table 16.1 Total consumption of J01 antibacterials by route of administration (2014)

Route of administration	DDD/1000 inhabitants per day[a] (% of total[b])											
	ALB	ARM	AZE	BLR	KGZ	KOS	MDA	MNE	SRB	TJK	TUR	UZB
Oral J01	21 (92)	12.9 (90)	2.6 (31)	16.7 (84)	28.7 (78)	18.8 (91)	14 (79)	31 (95)	27.8 (94)	27.7 (72)	38.7 (96)	6 (57)
Parenteral J01	1.8 (8)	1.5 (10)	5.8 (69)	3.3 (16)	8.1 (22)	2 (9)	3.7 (21)	1.7 (5)	1.7 (6)	11 (28)	1.7 (4)	4.5 (43)
Total	**22.7**	**14.4**	**8.5**	**20.0**	**36.8**	**20.8**	**17.7**	**32.7**	**29.5**	**38.7**	**40.4**	**10.4**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

16.2.2 Total consumption of J01 antibacterials by pharmacological subgroup

The consumption of J01 antibacterials by pharmacological subgroup is shown in Fig. 16.2 and summarized in Table 16.2.

Consistent with the variability in total consumption of J01 antibacterials, the absolute volumes of use of the pharmacological subgroups differed by setting. In each case, beta-lactams (J01C) was the most consumed of the subgroups, generally followed by cephalosporins (J01D) (Table 16.2).

[4] Abbreviations of country and area names used in some tables and figures in this chapter are as follows: ALB: Albania; ARM: Armenia; AZE: Azerbaijan; BLR: Belarus; KGZ: Kyrgyzstan; KOS: Kosovo (in accordance with Security Council resolution 1244 (1999)); MDA: Republic of Moldova; MNE: Montenegro; SRB: Serbia; TJK: Tajikistan; TUR: Turkey; UZB: Uzbekistan.

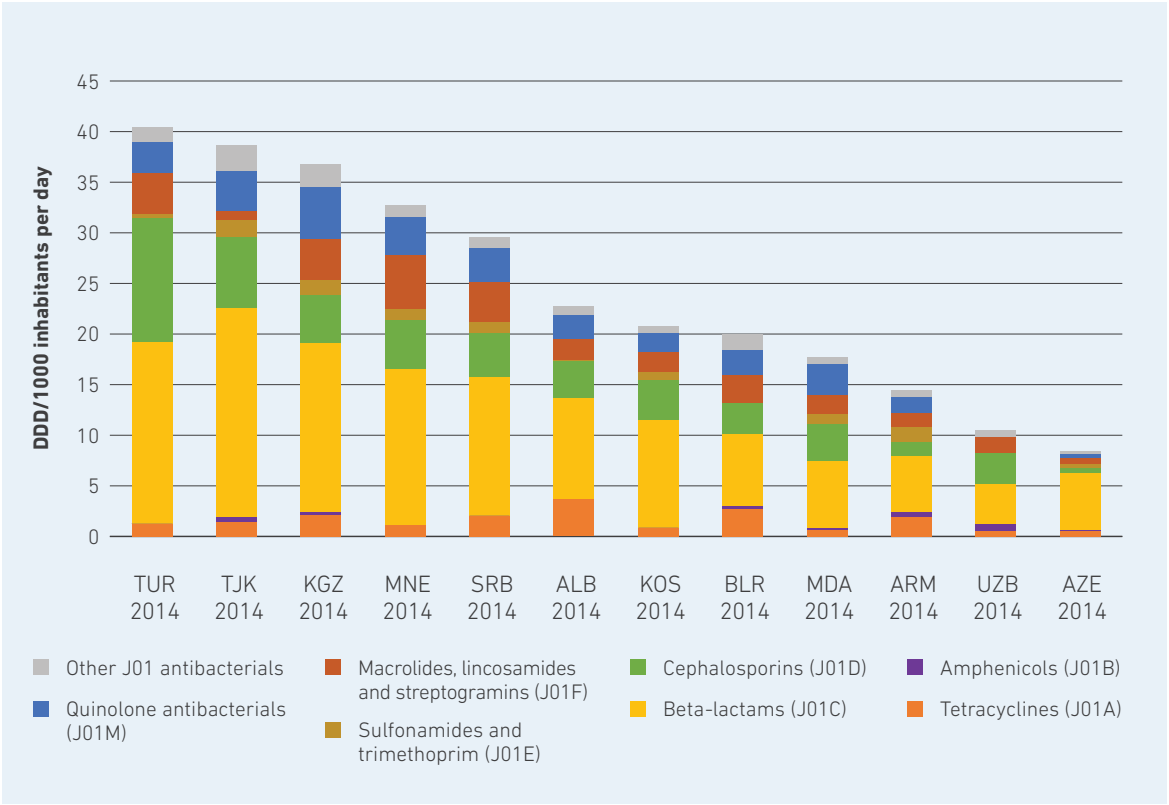

Fig. 16.2 Total consumption of J01 antibacterials by pharmacological subgroup (2014)

DDD: defined daily dose.

Table 16.2 Total consumption of J01 antibacterials by pharmacological subgroup (2014)

Class of antibacterial agents	DDD/1000 inhabitants per day[a]											
	ALB	ARM	AZE	BLR	KGZ	KOS	MDA	MNE	SRB	TJK	TUR	UZB
Tetracyclines (J01A)	3.6	2.0	0.6	2.7	2.1	0.9	0.6	1.1	2.1	1.4	1.3	0.5
Amphenicols (J01B)	0.1	0.4	0.1	0.2	0.3	<0.1	0.2	-	<0.1	0.5	<0.1	0.7
Beta-lactams (J01C)	9.9	5.6	5.6	7.1	16.7	10.6	6.6	15.4	13.7	20.7	18.0	3.9
Cephalosporins (J01D)	3.6	1.4	0.5	3.1	4.7	3.9	3.7	4.9	4.4	7.0	12.2	3.1
Sulfonamides and trimethoprim (J01E)	0.2	1.4	0.5	–	1.5	0.8	1.0	1.1	1.1	1.7	0.4	–
Macrolides, lincosamides and streptogramins (J01F)	2.0	1.4	0.6	2.8	4.1	1.9	1.9	5.3	3.9	0.9	4.1	1.6
Quinolone antibacterials (J01M)	2.4	1.5	0.4	2.5	5.0	1.9	3.0	3.7	3.3	4.0	3.0	<0.1
Other J01 antibacterials	0.8	0.7	0.3	1.6	2.4	0.7	0.7	1.2	1.0	2.6	1.5	0.6
Total[b]	**22.7**	**14.4**	**8.5**	**20.0**	**36.8**	**20.8**	**17.7**	**32.7**	**29.5**	**38.7**	**40.4**	**10.4**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

16.3 Relative consumption of J01 antibacterials

16.3.1 Relative consumption of J01 antibacterials by pharmacological subgroup

The relative consumption of pharmacological subgroups measured as a proportion of total J01 antibacterials is shown in Fig. 16.3 and summarized in Table 16.3.

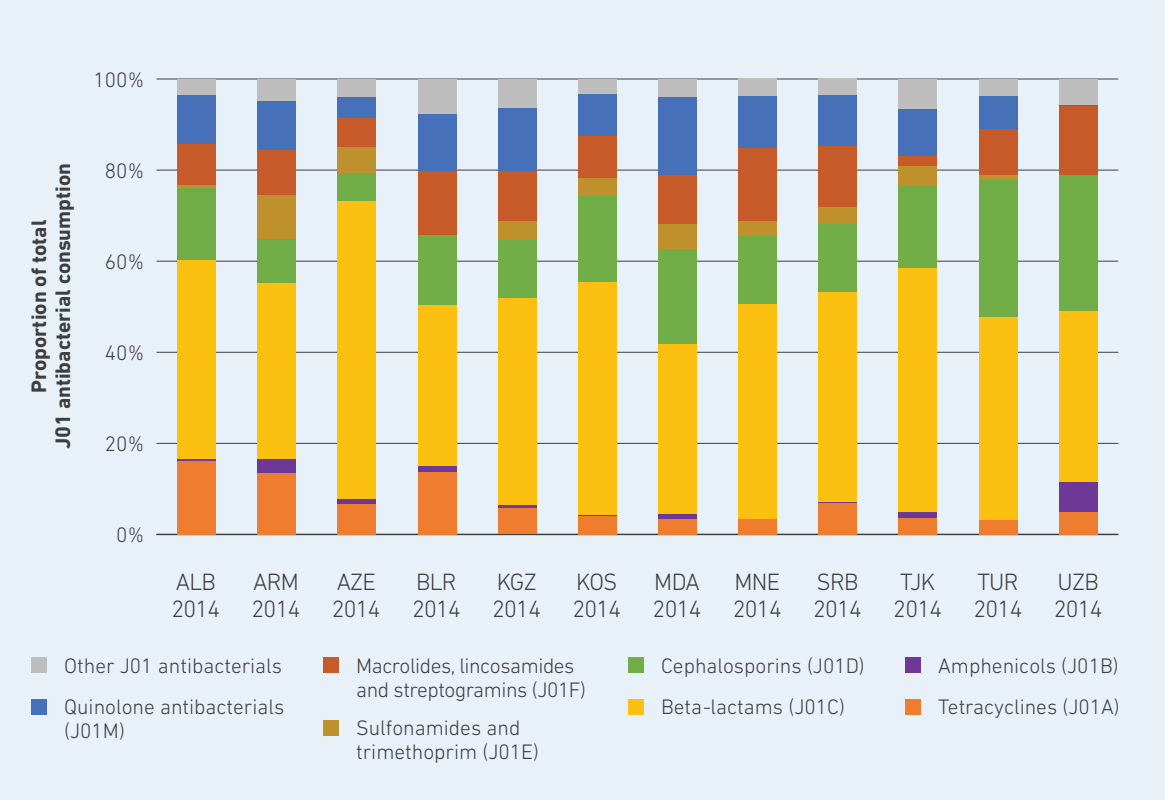

Fig. 16.3 Relative consumption of J01 antibacterials by pharmacological subgroup (2014)

The estimates of relative use of the J01 pharmacological subgroups illustrate the consumption patterns. Beta-lactams (J01C) constituted between 35.4% (Belarus) and 65.6% (Azerbaijan) of total consumption. Cephalosporins represented from 6.1% (Azerbaijan) to 30.3% (Turkey) of total consumption, while quinolones made up 17% of total J01 consumption in the Republic of Moldova and less than 0.1% in Uzbekistan (Table 16.3).

Table 16.3 Relative consumption of J01 antibacterials by pharmacological subgroup (2014)

Class of antibacterial agents	Consumption as proportion of total J01 consumption (%)[a]											
	ALB	ARM	AZE	BLR	KGZ	KOS	MDA	MNE	SRB	TJK	TUR	UZB
Tetracyclines (J01A)	16.0	13.5	6.7	13.7	5.7	4.1	3.4	3.4	7.0	3.7	3.1	5.0
Amphenicols (J01B)	0.4	2.9	0.9	1.2	0.8	<0.1	1.1	-	<0.1	1.2	<0.1	6.6
Beta-lactams (J01C)	43.7	38.8	65.6	35.4	45.4	51.2	37.3	47.0	46.2	53.5	44.5	37.5
Cephalosporins (J01D)	15.9	9.5	6.1	15.4	12.8	19.0	20.7	15.0	14.9	18.1	30.3	29.8
Sulfonamides and trimethoprim (J01E)	0.7	9.7	5.6	<0.1	4.0	3.9	5.6	3.3	3.6	4.3	0.9	–
Macrolides, lincosamides and streptogramins (J01F)	9.0	9.9	6.5	14.1	11.2	9.2	10.9	16.2	13.3	2.3	10.1	15.3
Quinolone antibacterials (J01M)	10.7	10.6	4.5	12.3	13.7	9.2	17.0	11.4	11.3	10.3	7.4	<0.1
Other J01 antibacterials	3.6	5.0	4.1	7.9	6.4	3.4	4.0	3.7	3.5	6.6	3.7	5.8

[a] Total percentages may vary slightly owing to rounding.

16.3.2 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials

The relative consumption of cephalosporins and quinolones measured as a percentage of total J01 antibacterials in 2014 is shown in Fig. 16.4 and summarized in Table 16.4.

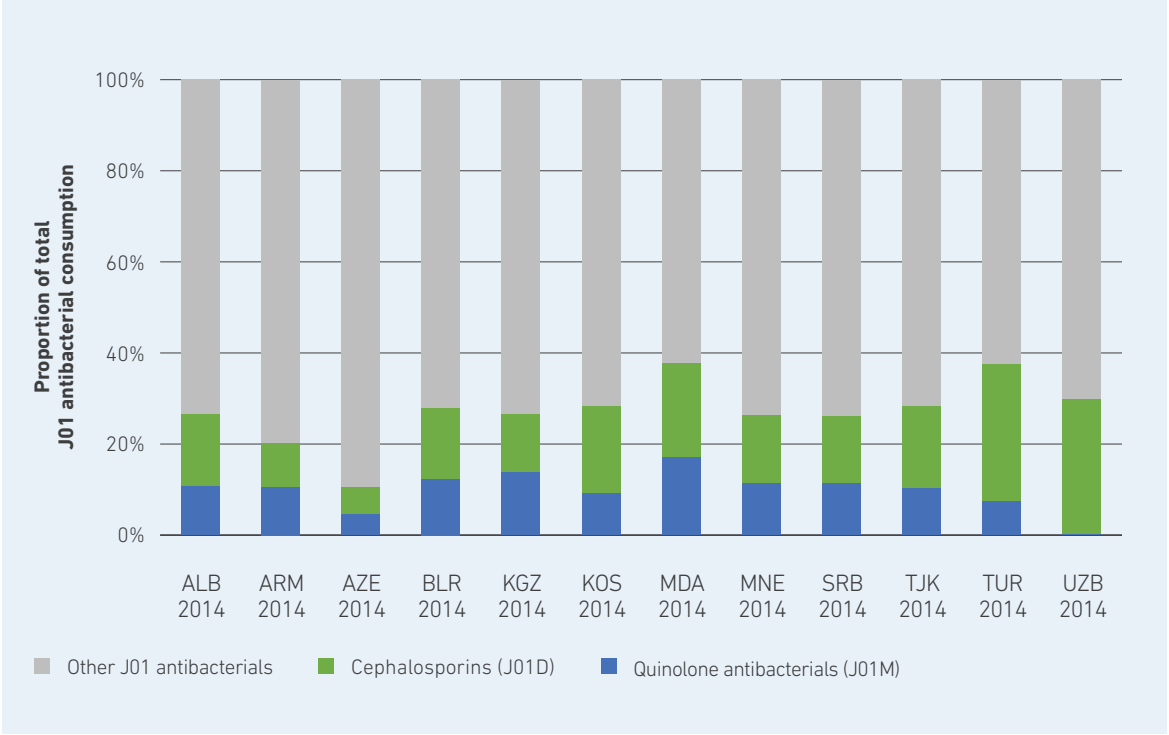

Fig. 16.4 Consumption of cephalosporins and quinolones as a percentage of the total consumption of J01 antibacterials (2014)

As noted in relation to Table 16.3, there was considerable variation in the use of the two pharmacological subgroups. Together, the two groups represented between 10% (Azerbaijan) and 38% (Republic of Moldova) of total J01 consumption (Table 16.4).

Table 16.4 Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials (2014)

Class of antibacterial agents	DDD/1000 inhabitants per day[a] (% of total[b])											
	ALB	ARM	AZE	BLR	KGZ	KOS	MDA	MNE	SRB	TJK	TUR	UZB
Quinolone antibacterials (J01M)	2.4 (11)	1.5 (11)	0.4 (4)	2.5 (12)	5 (14)	1.9 (9)	3 (17)	3.7 (11)	3.3 (11)	4 (10)	3 (7)	<0.1
Cephalosporins (J01D)	3.6 (16)	1.4 (10)	0.5 (6)	3.1 (15)	4.7 (13)	3.9 (19)	3.7 (21)	4.9 (15)	4.4 (15)	7 (18)	12.2 (30)	3.1 (30)
Other J01 antibacterials	16.7 (73)	11.5 (80)	7.6 (89)	14.4 (72)	27.1 (73)	14.9 (72)	11 (62)	24.1 (74)	21.8 (74)	27.7 (72)	25.2 (62)	7.3 (70)
Total	**22.7**	**14.4**	**8.5**	**20.0**	**36.8**	**20.8**	**17.7**	**32.7**	**29.5**	**38.7**	**40.4**	**10.4**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

16.4 Relative consumption by choice of agent

16.4.1 Relative consumption of cephalosporins by generation

The relative consumption of first-, second-, third- and fourth-generation cephalosporins in 2014 is shown in Fig. 16.5 and summarized in Table 16.5.

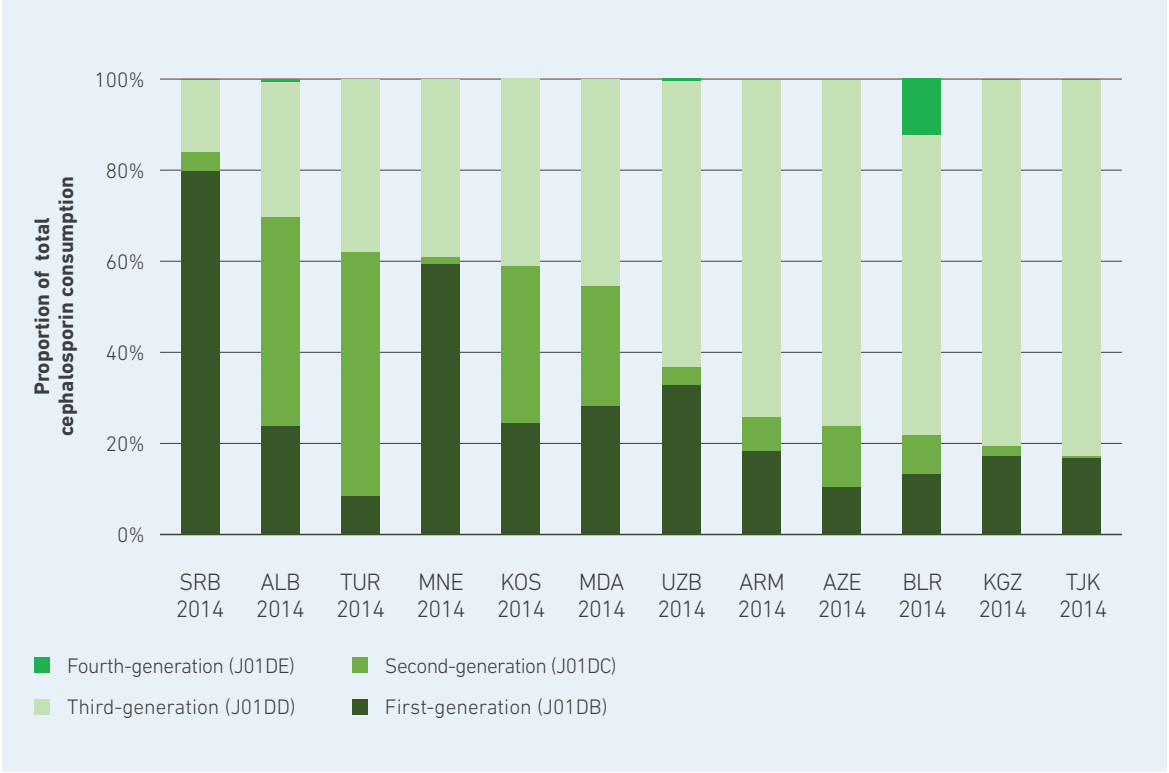

Fig. 16.5 Relative consumption of cephalosporins by generation (2014)

Fourth-generation cephalosporins were not widely consumed (mostly <0.1 DID).

Relative consumption of first-generation agents varied from 8% (Turkey) to 80% (Serbia), and second-generation agents from very low consumption (<0.1 DID) in a number of settings to 54% of cephalosporin consumption (6.5 DID) in Turkey.

Third-generation agent consumption ranged from 16% (Serbia) to 83% (Tajikistan) of total cephalosporin consumption and represented more than 50% of total consumption in six of the 12 datasets.

Table 16.5 Relative consumption of cephalosporins by generation (2014)

Generation	DDD/1000 inhabitants per day[a] (% of total[b])											
	ALB	ARM	AZE	BLR	KGZ	KOS	MDA	MNE	SRB	TJK	TUR	UZB
First-generation (J01DB)	0.9 (24)	0.2 (18)	<0.1	0.4 (13)	0.8 (17)	1 (25)	1 (28)	2.9 (59)	3.5 (80)	1.2 (17)	1 (8)	1 (33)
Second-generation (J01DC)	1.7 (46)	<0.1	<0.1	0.3 (9)	0.1 (2)	1.3 (34)	1 (26)	<0.1	0.2 (4)	<0.1	6.5 (54)	0.1 (4)
Third-generation (J01DD)	1.1 (30)	1 (74)	0.4 (76)	2 (66)	3.8 (80)	1.6 (41)	1.7 (45)	1.9 (39)	0.7 (16)	5.8 (83)	4.6 (38)	1.9 (63)
Fourth-generation (J01DE)	<0.1	<0.1	<0.1	0.4 (13)	<0.1	–	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
Total	**3.6**	**1.4**	**0.5**	**3.0**	**4.7**	**3.9**	**3.7**	**4.9**	**4.4**	**7.0**	**12.2**	**3.1**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

16.4.2 Relative consumption of amoxicillin, amoxicillin and clavulanic acid

The relative consumption of amoxicillin and the broader-spectrum amoxicillin and clavulanic acid is shown in Fig. 16.6 and summarized in Table 16.6.

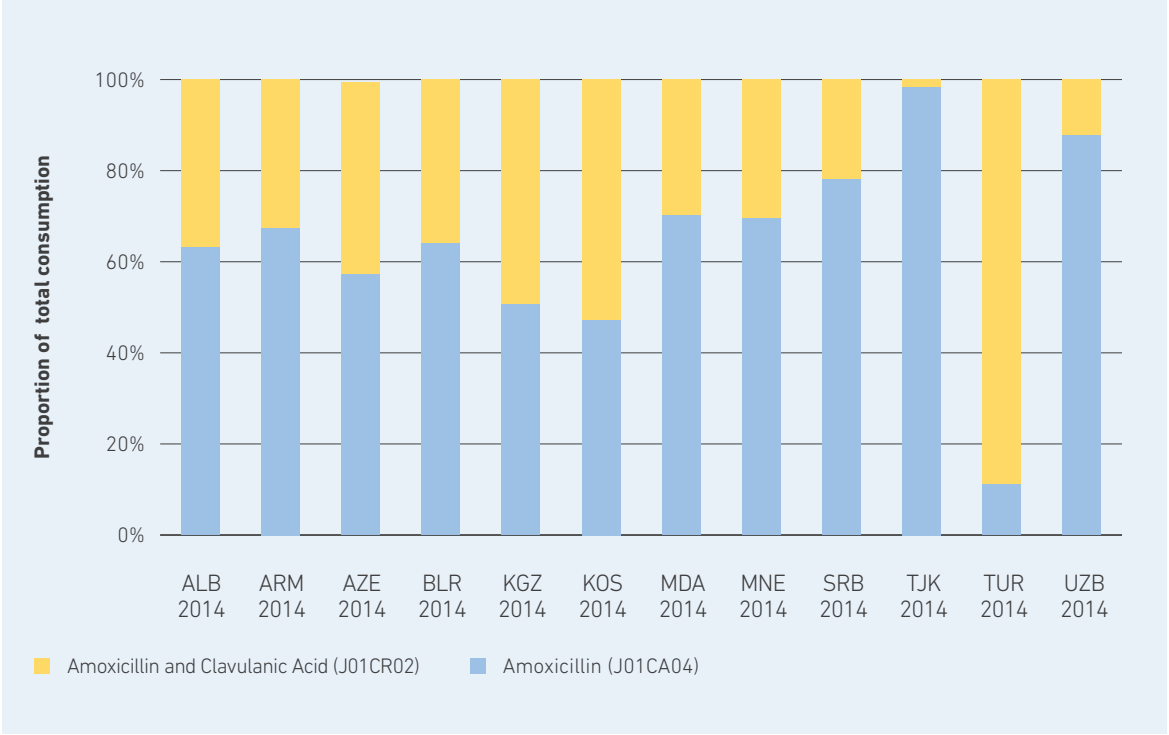

Fig. 16.6 Relative consumption of amoxicillin, amoxicillin and clavulanic acid (2014)

Amoxicillin was the more consumed agent in most datasets – the exception was Turkey, where only 11% of consumption was amoxicillin (Table 16.6).

Table 16.6 Relative consumption of cephalosporins by generation (2014)

Generation	DDD/1000 inhabitants per day[a] (% of total[b])											
	ALB	ARM	AZE	BLR	KGZ	KOS	MDA	MNE	SRB	TJK	TUR	UZB
Amoxicillin (J01CA04)	5.8 (63)	3.5 (67)	0.3 (57)	4.2 (64)	7.4 (51)	4.5 (47)	3.8 (70)	9.8 (70)	9.8 (78)	14.5 (98)	1.9 (11)	1.9 (88)
Amoxicillin and clavulanic acid (J01CR02)	3.4 (37)	1.7 (33)	0.2 (43)	2.4 (36)	7.3 (49)	5 (53)	1.6 (30)	4.3 (30)	2.7 (22)	0.2 (2)	15 (89)	0.3 (12)
Total	**9.1**	**5.2**	**0.5**	**6.6**	**14.7**	**9.5**	**5.5**	**14.1**	**12.5**	**14.7**	**16.8**	**2.2**

[a] DDD: daily defined dose. [b] Total amounts and percentages may vary slightly owing to rounding.

16.5 Comparisons with ESAC-Net antimicrobial quality indicators

ESAC-Net analyses use a number of metrics referred to as quality indicators (ECDC, 2017b). The measures in common in the ESAC-Net analysis and this report are shown in Annex 3.

Results for each measure are shown by separately country or area, along with the range of values for the WHO AMC Network and ESAC-Net 2014 analyses (Table 16.7).

Table 16.7 Quality indicators for antibiotic consumption for total care (2014)

Country or area	DDD/1000 inhabitants per day[a]					Relative consumption (%)	
	J01	J01C	J01D	J01F	J01M	J01DD+DE	J01MA
Albania	22.7	9.9	3.6	2.0	2.4	5	10
Armenia	14.4	5.6	1.4	1.4	1.5	7	10
Azerbaijan	8.5	5.6	0.5	0.6	0.4	5	4
Belarus	20.0	7.1	3.1	2.8	2.5	12	12
Kyrgyzstan	36.8	16.7	4.7	4.1	5.0	10	14
Montenegro	32.7	15.4	4.9	5.3	3.7	6	7
Republic of Moldova	17.7	6.6	3.7	1.9	3.0	9	16
Serbia	29.5	13.7	4.4	3.9	3.3	2	8
Tajikistan	38.7	20.7	7.0	0.9	4.0	15	10
Turkey	40.4	18.0	12.2	4.1	3.0	11	7
Uzbekistan	10.4	3.9	3.1	1.6	<0.1	19	<0.1
Kosovo (in accordance with United Nations Security Council resolution 1244 (1999))	20.8	10.6	3.9	1.9	1.9	8	8
WHO AMC Network results 2014							
Range of values	8.5–40.4	3.9–20.7	0.5–12.2	0.6–5.3	<0.1–5.0	2–19	<0.1–16
ESAC-Net results 2014							
Range of values	10.6–35.1	4.2–18.0	0.03–7.3	0.61–7.9	0.50–3.7	<0.1–7.0	2.3–14.9

Abbreviations: J01: antibacterials for systemic use; J01C: beta-lactams, penicillins; J01D: other beta-lactam antibacterials; J01F: macrolides, lincosamides and streptogramins; J01M: quinolone antibacterials; J01DD+DE: third- and fourth-generation cephalosporins; J01MA: fluoroquinolones
[a] DDD: daily defined dose.

Both datasets show considerable variability in these antibiotic quality indicators. One important difference between the data sets is that ESAC-Net data relate to the community sector, while WHO AMC Network data reflect total care. Nevertheless, in both cases the variability in overall consumption and for specific subgroups of antibacterials provides a basis for further national-level investigation into how these agents are consumed in practice.

17. DISCUSSION

This report aims to present the data collected through the WHO AMC Network, to provide guidance to countries and areas on building or strengthening their national AMC surveillance and to stimulate the sharing of data both nationally and internationally. A national approach to monitoring and evaluation provides centralized data to ensure that policies and strategies to address antimicrobial resistance are effective.

Data limitations must be acknowledged. The results presented are mostly based on import records and local manufacturer sales records. Some of the limitations of these sources are described in section 3.4. The completeness, validity and reliability of the data should be considered when interpreting the results of the analyses. A fuller interpretation of the consumption data requires an understanding of the local context, taking account of changes in regulations (including enforcement of prescription-only status), data sources, resistance patterns and the potential impact of interventions to change practices. This report includes a number of examples of interventions that have led to changes in practice.

The antimicrobial consumption data should be disseminated not only at the national level but also regionally and locally. All relevant stakeholders should be informed in order to help guide, inform and evaluate interventions for behaviour change, with the ultimate aims of improving appropriate use of antimicrobials and reducing antimicrobial resistance. Public reporting can be a positive way to inform patients and the community transparently about the importance of antimicrobial resistance and the role the community plays in appropriate use of antimicrobials. Sharing of information increases confidence that these are being taken seriously as key public health issues.

Problem practices need to be addressed and interventions to improve practice developed. This may require regulatory interventions, such as enforcing prescription-only status for antimicrobials. Regulatory agencies also have an important role in ensuring that only high-quality medicines are in circulation. Problems with substandard and falsified products require attention. The pharmaceutical industry also has a role to play. It is important to assess the impact of industry in promoting use of antimicrobials. In addition, the existence of local manufacturers of specific products may be an influence on observed patterns of consumption.

The quantitative data on antimicrobials in the report are a starting-point for further studies to understand better the use of these medicines in clinical practice – this will require further quantitative and qualitative studies in primary care and hospital sectors.

The data presented summarize the early experience of the WHO AMC Network. Despite some data limitations, the levels of AMC reported and in some cases the choices of antimicrobial agents used confirm the need for action. The variability between countries suggests that the differences in patterns of consumption are not solely related to differences in disease burden. A commitment to ongoing collection, analysis and use of consumption data is essential and is a central element laid out in the Global Action Plan adopted during the World Health Assembly in May 2015.

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ANNEX 1. METHODOLOGY

The WHO Antimicrobial Medicines Consumption (AMC) Network uses the Anatomical Therapeutic Chemical (ATC) classification system. The most commonly used measurement metric is the number of defined daily doses (DDD).

ATC classification system

The ATC classification system allows flexibility in reporting by medicine or group of medicines. Medicines are classified in groups at five different levels. The majority of antimicrobial agents are classified in ATC main group J: anti-infectives for systemic use.

Level 1 (main group)

Main group J	anti-infectives for systemic use

Level 2 (pharmacological/therapeutic subgroups)

ATC code	Name
J01	antibacterials for systemic use
J02	antimycotics for systemic use
J04	antimycobacterials
J05	antivirals for systemic use
J06	immune sera and immunoglobulins
J07	vaccines

Level 3 (chemical/pharmacological/therapeutic subgroups)

For example, within J01 these are:

ATC code	Name
J01A	tetracyclines
J01B	amphenicols
J01C	beta-lactam antibacterials, penicillins
J01D	other beta-lactam antibacterials
J01E	sulfonamides and trimethoprim
J01F	macrolides, lincosamides and streptogramins
J01G	aminoglycoside antibacterials
J01M	quinolone antibacterials
J01R	combinations of antibacterials
J01X	other antibacterials

Level 4 (chemical/pharmacological/therapeutic subgroups)

For example, within J01C these are:

ATC code	Name
J01CA	Penicillins with extended spectrum
J01CE	Beta-lactamase sensitive penicillins
J01CF	Beta-lactamase resistant penicillins
J01CG	Beta-lactamase inhibitors
J01CR	Combinations of penicillins, including beta-lactamase inhibitors

Level 5 (chemical substance)

For example, within J01CA, these are:

ATC code	Name
J01CA01	ampicillin
J01CA02	pivampicillin
J01CA03	carbenicillin
J01CA04	amoxicillin
J01CA05	carindacillin
J01CA06	bacampicillin
J01CA07	epicillin
J01CA08	pivmecillinam
J01CA09	azlocillin
J01CA10	mezlocillin
J01CA11	mecillinam

ATC code	Name
J01CA12	piperacillin
J01CA13	ticarcillin
J01CA14	metampicillin
J01CA15	talampicillin
J01CA16	sulbenicillin
J01CA17	temocillin
J01CA18	hetacillin
J01CA19	aspoxicillin
J01CA20	combinations
J01CA51	ampicillin, combinations

Unit of measurement: DDD

The DDD is the assumed average maintenance dose per day for a medicine used for its main indication in adults. A DDD is only assigned for medicines that already have an ATC code. The DDD, however, is only a technical unit of use and does not necessarily reflect the recommended or average prescribed daily dose. The DDDs for anti-infectives are as a rule based on use in infections of moderate severity, but some anti-infectives are only used in severe infections and their DDDs are assigned accordingly. There are no separate DDDs for children, which makes the DDD estimates for paediatric formulations more difficult to interpret.

The number of DDDs is calculated as follows:

$$\textbf{Number of DDDs} = \frac{\text{Total grams used}}{\text{DDD value in grams}}$$

Where the total grams of medicine used is determined by summing the amounts of active ingredient across the various formulations (different strengths of tablets or capsules, syrup formulations, injections etc.) and pack sizes.

The number of DDDs provides a measure of extent of use, but for comparative purposes these data are usually adjusted for population size or population group, depending on the medicines of interest and the level of data disaggregation that is possible.

For most antimicrobials, DDD per 1000 inhabitants per day (DID) are calculated for the total population, including all age and gender groups. It may also be possible to stratify national estimates.

ANNEX 2. DATA COLLECTION

Data sources of antimicrobial consumption data

Most countries and areas participating in the WHO Antimicrobial Medicines Consumption (AMC) Network use import data (data from customs records and declaration forms) as one of the sources of information on antimicrobial consumption. These are supplemented with sales records from market authorization holders or local manufacturing estimates where there is local pharmaceutical manufacturing.

It is very important to identify correctly the data sources used in the country. If more than one source is used, it is important to be aware of overlaps in the information provided. If they are treated as separate estimates and combined to provide "total consumption", this may overestimate actual antimicrobial consumption. Conversely, incomplete capture of import, wholesaler or manufacturing data may underestimate antimicrobial consumption by sector (community or hospital; public or private).

Table A2.1 summarizes some of the strengths and limitations of some of the different data sources.

Antimicrobial consumption data

Product-level data

The first step requires identification of all the products for the antimicrobial agents registered (i.e. those with marketing authorization) in the country – a valid national exhaustive register of products. The register file is updated each year as new products receive marketing authorization.

Package-level data

Consumption may be expressed as the total number of packages for each product in the register of antimicrobial products consumed during the defined period. These will mostly be annual data.

Analyses based on packages of medicines will provide a crude estimate of the number of courses of treatment with antimicrobials used per year, based on the assumption that one package = one course of treatment. This measure needs to be interpreted carefully. In some settings, a package of oral medicine will represent a course of treatment. In other settings, patients may buy small numbers of tablets or capsules, or dispensing may be from large containers of the medicine, in which case a package will have very little meaning. A package is not likely to be a good guide to a course of treatment with a parenteral (injectable) antimicrobial.

Substance-level data

Consumption at the substance level can be summarized as aggregated defined daily doses (DDDs). The DDD value is assigned by the WHO Collaborating Centre for Drug Statistics Methodology.

Table A2.1 Strengths and limitations of data sources for antimicrobial consumption

Data source	Strengths	Limitations
Import data	- Import permits are issued by government. - Records are centralized. - Reporting for customs declaration forms is standardized, including product type (generic, branded), volume, port of origin, country of manufacture, batch number and expiry date. - Data include over-the-counter medicines.	- Documentation may be incomplete. - Data may include parallel trade stock movements. - Data do not account for smuggled goods or illegal entry of products. - Volumes match import cycles not consumption patterns. - Records are administrative – not formatted for research and analysis.
Local manufacturers	- Local licensed producers should be easily identified. - Product volumes for local use and for export can be separated. - Data in a format suitable for analysis can be requested.	- Private companies may be unwilling to provide data. - Volumes reflect production not consumption patterns.
Wholesalers	- Only legal entities are able to import medicines for distribution. - Purchase and supply data can be provided. - Supply data may be disaggregated (by community/hospital, region, facility type). - Data collection is easier where numbers of wholesalers are limited. - Distribution/supply data are likely to be closer to actual consumption than purchase data.	- In some countries medical, dental and veterinary practitioners and pharmacists can also import medicines. - It may be difficult to get data from the private sector. - Numbers of wholesalers are high in some settings. - Some may supply other smaller wholesalers rather than end-users. - Wholesalers may provide agriculture and veterinary sectors as well as medicines for human use.
Commercial data sources (such as IMS Health)	- Data collection is standardized. - There is capacity to combine data from multiple sources including manufacturer records, hospital and pharmacy data.	- Data must be purchased. - Data collection may be limited in some countries. - It may not be possible to examine data at regional, local, facility or prescriber level. - Data may use classification other than Anatomical Therapeutic Chemical (ATC) codes, so information at the pharmacological or chemical subgroup level may be limited.

Population estimates

For this report, population estimates were mostly obtained from the World Bank database (World Bank, 2016). These data are regularly updated and the population numbers can change. It is therefore important to note the source and date of the data used. For calculations of 2011–2013 consumption data, World Bank population estimates updated on 7 January 2015 were used. For calculations of 2014 consumption data, World Bank population estimates updated on 14 October 2016 were used.

National population estimates may differ from World Bank estimates and the use of national population data may give slightly different estimates of population-adjusted consumption expressed as DDD per 1000 inhabitants per day (DID). These differences in population estimates do not affect the calculations of relative consumption of pharmacological subgroups or groups of agents.

Template for data collection

Data collection for the WHO AMC Network follows a standardized protocol and uses a common Excel data collection template.

A list of all antimicrobial medicines registered in the country (i.e. those with marketing authorization) is created. The route of administration (oral, parenteral, rectal, inhalation powder, inhalation solution) is entered to facilitate separate analyses such as for oral and parenteral formulations.

Each product is identified by the relevant ATC code and level. The DDD assigned by the WHO Collaborating Centre for Drugs Statistics Methodology (2016) with its unit of measurement (gram, milligram, millions of units) is entered alongside the product. The Centre also provides a list of combination products that have an approved DDD or "unit dose" measurement.

Data are entered for the number of packages for each registered product.

Population data are entered – this is the population for which the given consumption data apply. The total population may be based on WHO national population estimates for the relevant year or local estimates if there are reasons to believe that WHO estimates are inaccurate.

Contextual information related to antimicrobial consumption is entered into a separate worksheet, indicating whether the data represent the total, community or hospital consumption of antimicrobials.

Data verification

Validation of AMC data consists of two steps. The macro embedded in the template detects missing compulsory data and incorrect data units. The regional team reviews the submitted spreadsheets to identify other possible errors that cannot be detected by the macro. These include inconsistencies between data entered and product label information, unrealistic or improbable strengths of antimicrobials and miscalculated strengths of combination products when converted to standardized units. Errors are corrected by the regional team whenever possible, and the modified data sheets are returned to the AMC focal points for their confirmation and acceptance of any proposed changes. Potential errors that require more detailed product information or data requiring clarification are discussed with and corrected by the AMC focal points, and the modified data sent to the regional team again.

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ANNEX 3. MEASUREMENT METRICS AND QUALITY INDICATORS FOR ANTIMICROBIAL CONSUMPTION

As noted in section 3.3, this report focuses on a small number of measures of antibacterial consumption that are used to examine trends over time within countries and areas and in cross-national comparisons. The main types of key measure are:

- volume of consumption measures, reported as numbers of defined daily doses per 1000 inhabitants per day (DID);
- relative consumption measures, expressed as a percentage of total use of a group of antimicrobials;
- the agents consumed, reflecting the choice of specific antimicrobial agents within a class and allowing some more focused assessment of whether the choices align with recommended best practices and clinical practice guidelines.

Table A3.1 summarizes the measures reported and the relevant Anatomical Therapeutic Chemical (ATC) codes used in their calculation.

In addition, the report includes summaries of the utilization of the 10 most consumed agents (oral and parenteral formulations separately), along with the cumulative utilization these represent. This allows assessment of metrics such as which agents contribute to 75% of total drug utilization (DU75%). Often six or fewer agents make up the DU75%, and this potentially allows targeting of interventions to improve prescribing practices to these high-consumption medicines.

The 2012 European Surveillance on Antimicrobial Consumption Network (ESAC-Net) report (ECDC, 2014) noted that more than 50% of consumption of antibacterials for systemic use (ATC group J01) in the community was made up of 12 different antibacterial agents. In 22 (73%) of the 30 EU/European Economic Area countries included, three or fewer different agents were responsible for more than 50% of consumption of J01 antibacterials.

The ESAC-Net report makes no distinction in the use of oral and parenteral (injectable) formulations, and results relate to community use of antibacterials. In this WHO Antimicrobial Medicines Consumption (AMC) Network report, most data apply to total care; therefore, analyses are presented separately for oral and parenteral formulations.

Table A3.1 Metrics used in country-level analyses over time and cross-national comparisons

Category		Unit
Estimates of volumes of consumption of antibacterials for systemic use (J01)		
Total consumption of J01 antibacterials by route of administration	Oral J01 Parenteral J01	DID[a]
Total consumption of J01 antibacterials by pharmacological subgroup: - tetracyclines (J01A) - amphenicols (J01B) - beta-lactams (J01C) - cephalosporins (J01D) - sulfonamides and trimethoprim (J01E) - macrolides, lincosamides and streptogramins (J01F) - quinolone antibacterials (J01M) - other J01 antibacterials (J01G, J01R, J01X)	J01A, J01B, J01C, J01D, J01E, J01F, J01M, J01G, J01R, J01X	DID
Relative consumption of J01 antibacterials by subgroup		
Relative consumption of J01 antibacterials by pharmacological subgroup	J01A, J01B, J01C, J01D, J01E, J01F, J01M, (J01G + J01R + J01X) as % of J01	%
Consumption of cephalosporins and quinolones as a proportion of total consumption of J01 antibacterials	(J01DB +J01DC + J01DD + J01DE)/J01, J01M/J01	%
Relative consumption by choice of agent		
Relative consumption of agents of cephalosporins by generation	J01DB, J01DC, J01DD, J01DE as % of total cephalosporins	%
Relative consumption of cephalosporins by generation: - choice of first-generation cephalosporins (J01DB) - choice of second-generation cephalosporins (J01DC) - choice of third-generation cephalosporins (J01DD) - choice of fourth-generation cephalosporins (J01DE)	J01DB, J01DC, J01DD, J01DE as % of J01	%
Relative consumption of agents within fluoroquinolones (J01MA)	J01MA/J01	%
Relative consumption of amoxicillin and amoxicillin and clavulanic acid	J01CR02, J01CA04 as % of (J01CA04 + J01CR02)	%
The 10 most consumed agents		
The 10 most consumed agents – oral formulation	J01	DID
The 10 most consumed agents – parenteral formulation	J01	DID

[a] DID: DDD/1000 inhabitants per day.

Quality indicators for antimicrobial consumption

Quality indicators are defined as "measurable items of antibiotic use giving a possible indication of the level of quality, focusing on different aspects of quality (effectiveness, safety, appropriateness and costs, compliance, and persistence) and relevant to clinical practice" (Coenen et al., 2007).

Drug-specific quality indicators for outpatient use in Europe

The European Surveillance of Antimicrobial Consumption (ESAC) project developed 12 indicators of antibiotic use in 2007 (Coenen, 2007). These were identified from 22 initial indicators through a series of workshops with 27 experts from 15 European countries. The indicators are process indicators; they are comparative indicators with no link to thresholds that indicate appropriate levels of prescribing. They can be calculated with routinely gathered macro-level data.

Table A3.2 ESAC consensus-based antimicrobial quality indicators

Consumption			Included in this report
J01	J01_DID	Consumption of J01 antibacterials expressed in DID[a]	Yes
J01C	J01C_DID	Consumption of penicillins (J01C) expressed in DID	Yes
J01D	J01D_DID	Consumption of cephalosporins (J01D) expressed in DID	Yes
J01F	J01F_DID	Consumption of macrolides, lincosamides and streptogramins (J01F) expressed in DID	Yes
J01M	J01M_DID	Consumption of quinolones (J01M) expressed in DID	Yes
Relative consumption			
J01CE	J01CE_%	Consumption of beta-lactamase sensitive penicillins expressed as percentage	No
J01CR	J01CR_%	Consumption of combination of penicillins, including beta-lactamase inhibitor expressed as percentage	No
J01DD+DE	J01DD+DE_%	Consumption of third- and fourth-generation cephalosporins (J01DD+DE) expressed as percentage	Yes
J01MA	J01MA_%	Consumption of fluoroquinolones (J01MA) expressed as percentage	Yes
J01	J01_B/N	Ratio of the consumption of broad (J01(CR+DC+DD+(F-FA01))) to the consumption of narrow-spectrum penicillins, cephalosporins and macrolides (J01(CE+DB+FA+01))	No
J01	J01_SV	Seasonal variation of the total antibiotic consumption	No
J01M	J01M_SV	Seasonal variation of quinolone consumption multiplied by their use in DID	No

[a] DID: DDD/1000 inhabitants per day.

Table A3.2 shows the 12 ESAC antimicrobial quality indicators and indicates which of them are included in this report. A summary of antimicrobial quality indicators is also presented in Chapter 16.

Measures of seasonal variation in antimicrobial consumption are not included in the analyses as most consumption estimates are based on import and manufacturer records. It may be possible to examine seasonal variation in demand for antimicrobials in settings where consumption estimates are derived from data on wholesaler supplies to health facilities, or where health facility or prescribing data are available.

Disease-specific quality indicators for outpatient antibiotic prescribing

Following on from the consensus-based antimicrobial quality indicators developed for outpatient antibiotic use, ESAC has now developed a series of disease-specific indicators (Adriaenssens et al., 2011). This was in response to clinicians' need to have disease-specific, rather than drug-specific, information on antibiotic use. Using a similar process to that used for the previous indicators, the group developed seven broad indicators, each with two or three subindicators (Table A3.3).

These are also all process indicators, but unlike the previous ESAC indicators, the disease-specific indicators have recommended targets for use. Calculation of each of these indicators requires data linkage to the indications for use, and thus requires micro-level data collection.

While none of these indicators is included in this report, information on these measures is added below to illustrate future directions for analyses of antibacterial medicines, as data sources linking medicine with indication for treatment become available.

Table A3.3 Disease-specific quality indicators

Indicator number	Title	ATC code	Acceptable range (%)
1a	Percentage of patients aged between 18 and 75 years with acute bronchitis/bronchiolitis prescribed antibacterials for systemic use	J01	0–30
1b	=1a[a] receiving the recommended antibacterials	J01CA or J01AA	80–100
1c	=1a receiving quinolones	J01M	0–5
2a	Percentage of patients older than 1 year with acute upper respiratory infection prescribed antibacterials for systemic use	J01	0–20
2b	=2a receiving the recommended antibacterials	J01CE	80–100
2c	=2a receiving quinolones	J01M	0–5
3a	Percentage of female patients older than 18 years with cystitis/other urinary infection prescribed antibacterials for systemic use	J01	80–100
3b	=3a receiving the recommended antibacterials	J01XE or J01EA or J01XX	80–100
3c	=3a receiving quinolones	J01M	0–5
4a	Percentage of patients older than 1 year with acute tonsillitis prescribed antibacterials for systemic use	J01	0–20
4b	=4a receiving the recommended antibacterials	J01CE	80–100
4c	=4a receiving quinolones	J01M	0–5
5a	Percentage of patients older than 18 years with acute/chronic sinusitis prescribed antibacterials for systemic use	J01	0–20
5b	=5a receiving the recommended antibacterials	J01CA or J01CE	80–100
5c	=5a receiving quinolones	J01M	0–5
6a	Percentage of patients older than 2 years with acute otitis media/myringitis prescribed antibacterials for systemic use	J01	0–20
6b	=6a receiving the recommended antibacterials	J01CA or J01CE	80–100
6c	=6a receiving quinolones	J01M	0–5
7a	Percentage of patients aged between 18 and 65 years with pneumonia prescribed antibacterials for systemic use	J01	90–100
7b	=7a receiving the recommended antibacterials	J01CA or J01AA	80–100
7c	=7a receiving quinolones	J01M	0–5

Source: Adriaenssens et al. (2011).

[a] Of those aged between 18 and 75 years with acute bronchitis/bronchiolitis prescribed antibacterials for systemic use (1a), this represents the proportion that received recommended antibacterials. This notation is used throughout the table.

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The WHO Regional Office for Europe

The World Health Organization (WHO) is a specialized agency of the United Nations created in 1948 with the primary responsibility for international health matters and public health. The WHO Regional Office for Europe is one of six regional offices throughout the world, each with its own programme geared to the particular health conditions of the countries it serves.

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