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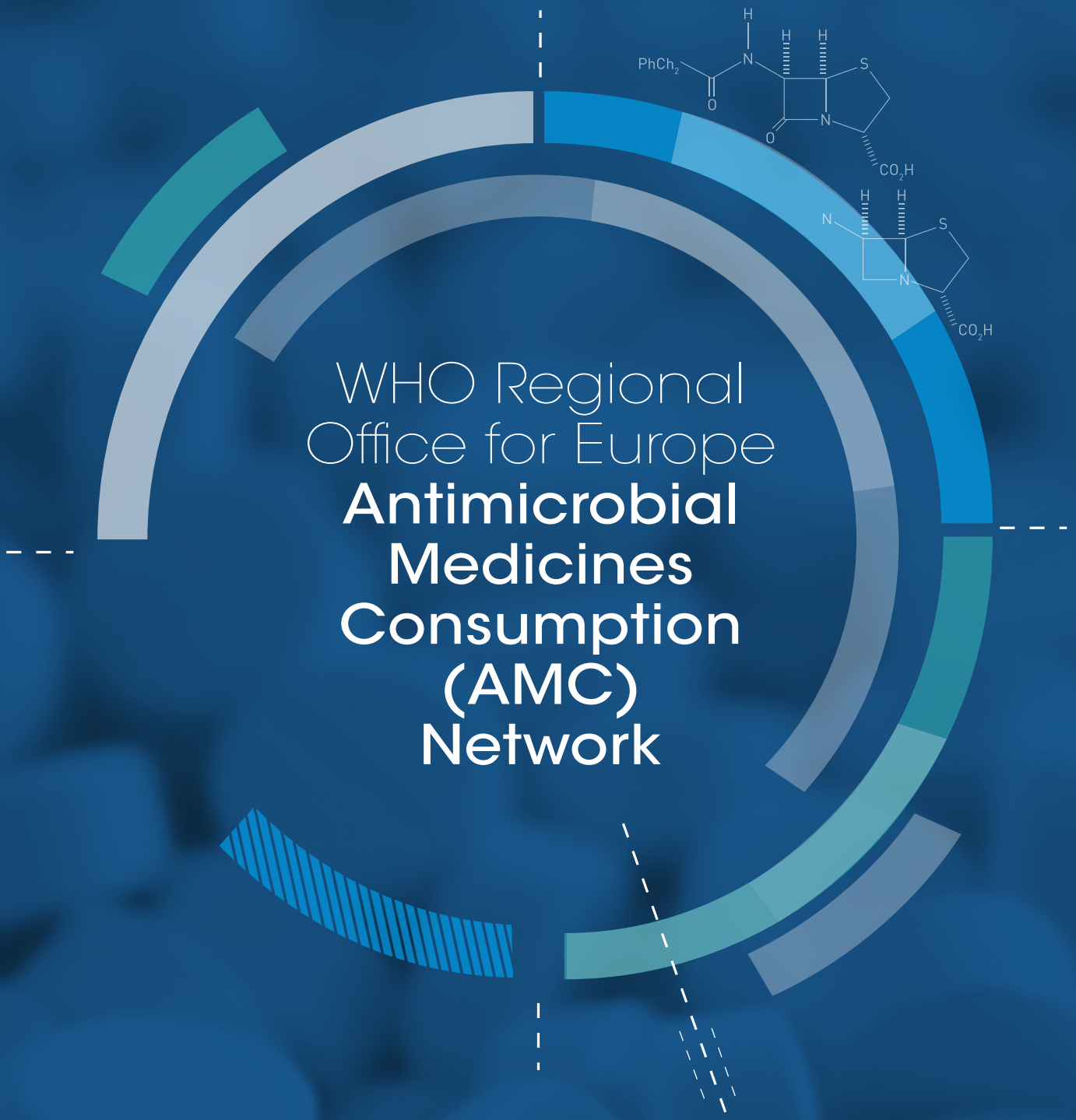

WHO Regional Office for Europe Antimicrobial Medicines Consumption (AMC) Network

AMC data 2019

Abstract

This report presents analyses of data on antimicrobial medicines consumption collected for 2019 from 14 non-European Union countries in the WHO European Region. The analyses incorporate the most recent changes to the WHO Access, Watch and Reserve (AWaRe) classification in 2021, and the report considers metrics to inform the responsible use of antibiotics. The WHO Regional Office for Europe and its partners remain committed to supporting countries/areas in these endeavours through the activities of the WHO Europe Antimicrobial Medicines Consumption (AMC) Network.

Keywords

ANTI-INFECTIVE AGENTS – THERAPEUTIC USE
ANTIBACTERIAL AGENTS
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ABBREVIATIONS

AMC	Antimicrobial Medicines Consumption (Network)
ANOVA	analysis of variance (test)
ATC	Anatomical Therapeutic Chemical (classification system)
AWaRe	WHO Access, Watch and Reserve (classification)
CAGR	compound annual growth rate
DDD	defined daily dose
DID	defined daily doses per 1000 inhabitants per day
DU75%	drug utilization 75%
ECDC	European Centre for Disease Prevention and Control
EML	WHO Model List of Essential Medicines for adults
EMLc	WHO Model List of Essential Medicines for children
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
EU	European Union

Abbreviations of country names used in some tables and figures

ALB	Albania
ARM	Armenia
AZE	Azerbaijan
BIH	Bosnia and Herzegovina
BLR	Belarus
GEO	Georgia
KAZ	Kazakhstan
KGZ	Kyrgyzstan
MDA	Republic of Moldova
MKD	North Macedonia
MNE	Montenegro
RUS	Russian Federation
SRB	Serbia
SWI	Switzerland
TJK	Tajikistan
TUR	Türkiye
UKR	Ukraine
UZB	Uzbekistan

EXECUTIVE SUMMARY

The WHO Europe Antimicrobial Medicines Consumption (AMC) Network aims to support all countries/areas 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). Members of the AMC Network comprise: Albania, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Georgia, Kazakhstan, Kyrgyzstan, Montenegro, North Macedonia, the Republic of Moldova, the Russian Federation, Serbia, Switzerland, Tajikistan, Türkiye, Ukraine and Uzbekistan, as well as Kosovo.[1]

This is the fourth AMC Network report. It sets out and analyses AMC data for 14 of the Network countries where the ministry of health approved data-sharing and publication. Data were not available from all countries/areas for all years of analysis. The report includes cross-national analyses of trends over time (2014–2019) for key metrics of antibacterial consumption, applies the 2021 WHO Access, Watch and Reserve (AWaRe) classification of antibiotics and reports on the WHO national monitoring target of at least 60% of total consumption being Access agents. Data are presented on the antibacterial substances accounting for 75% of consumption (the drug utilization 75% (DU75%)) measured in defined daily doses (DDD), and was calculated for oral and parenteral formulations separately.

Key findings

Data on total consumption of antibacterials for systemic use (Anatomical Therapeutic Chemical (ATC) classification group J01) were available for 14 countries in 2019. There was large variability in reported consumption of J01 antibacterials across the AMC Network – ranging from 10.6 defined daily doses per 1000 inhabitants per day (DID) (Switzerland) to 33.2 DID (Türkiye), with a median consumption of 19.6 DID. The population-weighted mean consumption across the 14 datasets was 21.2 DID. Consumption estimates were slightly higher than those reported in 2018.

The extent of consumption of parenteral formulations in 2019 varied from 5% in Türkiye to 49% in Kyrgyzstan. Two other countries reported parenteral consumption of more than 20% of total J01 consumption – Tajikistan (24%) and Uzbekistan (30%). There was considerable variation in the extent of consumption of the pharmacological subgroups of J01. In 2019, consumption of beta-lactam penicillins (J01C) ranged from 17% of J01 consumption in Kyrgyzstan to 42% in Türkiye and Bosnia and Herzegovina, and 43% in North Macedonia. Cephalosporin (J01D) consumption varied from 6% of J01 consumption in Azerbaijan to 38% in Kyrgyzstan. Quinolone (J01M) consumption varied from 7% in Montenegro to 28% in Tajikistan.

An analysis of trends over time showed statistically significant increases in total consumption of J01 antibacterials between 2014 and 2019 in two countries, namely Azerbaijan (+13.8%) and the Russian Federation (+3.2%). Increases in Azerbaijan were from a low baseline consumption of 6.4 DID in 2014.

Access agents represented between 35% (Uzbekistan) and 71% (Azerbaijan) of total antibacterial consumption in 2019. Conversely, consumption of Watch group agents represented between 28% (Azerbaijan) and 58% (Uzbekistan) of total consumption. Consumption of Reserve agents remained

1 All references to Kosovo in this publication should be understood to be in the context of United Nations Security Council resolution 1244 (1999).

low in all 14 countries. Unclassified agents constituted 4% of consumption in North Macedonia and 7% of consumption in Uzbekistan. The 2019 population-weighted estimates across the AMC Network were: Access agents 50.6%; Watch agents 46.7%; Reserve agents 0.2%; and unclassified agents 2.5%. In 2018, the comparable estimates were 46.9%, 49.5%, 0.1% and 3.5%.

In 2019, five AMC Network countries met WHO's suggested national target of 60% of total consumption of antibacterials being derived from the Access list. Bosnia and Herzegovina was the only AMC Network country to achieve this target in each of the six years analysed (2014–2019).

The number of agents constituting the DU75% – by oral substance – ranged from 5 to 10 across the AMC Network countries. There were 10 agents in the population-weighted DU75% for the AMC Network in 2018 – four Access and six Watch agents. The Watch agents ciprofloxacin and azithromycin were ranked three and four in relative consumption across the AMC Network. The Watch agent ceftriaxone was ranked number one for consumption of parenteral agents in nine countries and ranked second in three countries.

The results presented in this report document trends in consumption of antibacterial agents across the AMC Network. The results show wide variability of estimates, both in volumes of consumption and selection of agents, with increased consumption compared to 2018 estimates. Despite some data limitations, the levels of consumption reported and, in some cases, the choices of antimicrobial agents used confirm the need for action. While the quantitative metrics presented have limited application in assessing the appropriateness of prescribing, they illustrate differing patterns of antibacterial consumption over time and point to potential problems in antibiotic use.

Analyses based on the WHO AWaRe classification can support antimicrobial stewardship efforts and focus attention on prescribing practices that should be reviewed further. In 2019, five countries met the WHO proposed global monitoring indicator that 60% of all antibiotics consumed should come from the Access group, the group of antibiotics at lowest risk of resistance. The relatively higher levels of consumption of specific Watch group antibiotics identified in the DU75% analyses suggest some targets for further investigation, interventions and stewardship activities supported by evidence-based guidelines and treatment algorithms. Population-weighted estimates showed increased relative consumption of Access antibiotics and decreased relative consumption of Watch agents in 2019 compared to 2018.

The cross-national analyses presented focus on total consumption of antibacterials and facilitate benchmarking of activities across the AMC Network. Disaggregation of data to hospital and community sectors was not possible in most AMC Network countries/areas; this is an important area for future development. Disaggregation of data to community and hospital sectors facilitates the development of sector-specific interventions to increase the appropriateness of use of antibiotics.

As noted in previous AMC Network reports, the quantitative estimates presented here provide 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.

1. INTRODUCTION

1.1 Background

Ensuring prudent antimicrobial use is a key priority in an effective response to the challenges of antimicrobial resistance. The importance of surveillance of antibiotic consumption to identify potential overuse, underuse and inappropriate use is highlighted in the Global Action Plan on Antimicrobial Resistance (WHO, 2015), the European Strategic Action Plan on Antibiotic Resistance (WHO Regional Office for Europe, 2011) and the European One Health Action Plan against Antimicrobial Resistance (European Commission, 2017).

1.2 The WHO Europe AMC Network

The WHO Europe Antimicrobial Medicines Consumption (AMC) Network has been undertaking systematic surveillance of antimicrobial medicines consumption in 18 non-European Union (EU) Member States and an area, Kosovo,[2] since 2011 (WHO Regional Office for Europe, 2020). Data collection is based on the WHO Anatomical Therapeutic Chemical (ATC) classification system and defined daily doses (DDD) methodology (WHO Collaborating Centre for Drug Statistics Methodology, 2020).

The following countries/areas are currently engaged in the AMC Network: Albania, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Georgia, Kazakhstan, Kyrgyzstan, Montenegro, North Macedonia, the Republic of Moldova, the Russian Federation, Serbia, Switzerland, Tajikistan, Türkiye, Ukraine and Uzbekistan, as well as Kosovo.[2]

1.3 Previous publications of WHO Europe AMC Network data

A report of AMC Network data for 2011–2014 for 11 of the participating AMC Network countries and for Kosovo[2] was published in 2017 (WHO Regional Office for Europe, 2017).

A cross-national comparison of 2015 AMC data for 16 members of the AMC Network was published in 2019 (Robertson et al., 2019). This analysis classified consumption data according to the 2017 WHO Access, Watch and Reserve (AWaRe) classification of antibiotics (WHO, 2017a) and examined the implications of proposed changes to DDDs for some commonly used antibiotics that were to come into force in January 2019 (WHO Collaborating Centre for Drug Statistics Methodology, 2020).

An analysis of data for 2011–2017 for 17 Network members was also published in 2020 (WHO Regional Office for Europe, 2020).

A third report of AMC Network data (for 2014–2018) was published in 2021 (WHO Regional Office for Europe, 2021), as was a comparison of AMC Network data with that of the European Surveillance of Antibiotic Consumption Network (ESAC-Net) coordinated by the European Centre for Disease Prevention and Control (ECDC) using data for 2014–2019 (Robertson et al., 2021).

2 All references to Kosovo in this document should be understood to be in the context of United Nations Security Council resolution 1244 (1999).

1.4 Scope and aim of this report

This report extends the reporting of the WHO Europe AMC Network, presenting 2019 data for 14 Network countries where the ministries of health gave permission for their data to be published. Only cross-national comparisons are presented, and – where appropriate – comparisons with 2018 consumption data are made.

In most of the countries/areas participating in the AMC Network, it is not possible to disaggregate data by sector (community or hospital; public or private), so total consumption data are reported. Only five countries – Kazakhstan, Montenegro, the Russian Federation, Switzerland and Türkiye – currently are able to report disaggregated data.

The analyses apply the 2021 update of the AWaRe classification of antibiotics (WHO, 2021; see section 2.4.3), and assess concordance with the WHO global/national target that 60% of total consumption is Access agents (WHO Executive Board, 2018). In addition, analyses report on the antibacterial substances accounting for 75% of consumption – the drug utilization 75% (DU75%) (Zarb et al., 2011).

2. METHODS

2.1 Data sources and data collection

2.1.1 Data sources

Participating WHO Europe AMC Network countries/areas mostly rely on import data – using customs records and declaration forms – supplemented with sales records from market authorization holders, local manufacturing estimates, wholesaler records and, in some cases, commercial data sources – for deriving estimates of consumption (Table 2.1). Increasingly, data on antimicrobial use are available from health insurance programmes.

Table 2.1 Sources of data used for consumption estimates, 2014–2019

Country	2014	2015	2016	2017	2018	2019
Albania	I	I	I	I	I	–
Armenia	I, M	I, M	I, M	I, M	I, M	I, M
Azerbaijan	I	I	I	I	I	I
Belarus	I, M	I, M	I, M	I, M	I, M	I, M
Bosnia and Herzegovina	S	S	S	S	S	S
Georgia	I	I	I	I	I	I
Kazakhstan	–	S	S	S	S	–
Kyrgyzstan	–	I, S	I, S	I, S	I, S	I, S
Montenegro	S	S	S	S	S	S
North Macedonia[a]	R	R	R	R	R	R
Republic of Moldova	I, M	I, M	I, M	I, M	I, M	–
Russian Federation	S	S	S	S	S	S
Serbia	S	S	S	S	S	S
Switzerland[b]	–	–	–	S	S	S
Tajikistan	I, C	I, C	I, C	I, C	I, C	I, C
Türkiye[c]	S	S	S	S	S	S
Ukraine	S	S	S	S	S	–
Uzbekistan	–	–	I, S	I, S	I, S	I, S

C: certification records; I: import records; M: manufacturing records; R: reimbursement data; S: sales data.
[a] Reimbursement data cover the community sector only. [b] Estimates derived from IQVIA data based on sales from distributors to pharmacies, self-dispensing doctors and hospital, therefore covering outpatient and inpatient consumption. [c] Türkiye uses wholesalers' records from the pharmaceutical track and trace system.
Source: AMC Network.

Most network countries have established data collection methods that have been used in analyses and described in previous AMC reports. Switzerland, which is new to the network, has provided data for each of the six years of data collection (2014–2019), but data collection is partial for some years. Data in the Swiss Antibiotic Resistance Report 2020 (Federal Office of Public Health and Federal Food Safety and Veterinary Office, 2020) covers 2017, 2018 and 2019 and these are used for this report as they represent total consumption estimates. Estimates are obtained from IQVIA.[3]

3 IQVIA is a human data science company which has assets in data, technology and advanced analytics with an interest in health care and human health.

In the case of Ukraine, access to consumption data has been difficult and data sources have changed over time. The main sources of data for the country are a market research company, Proxima Research, and include government tenders for the hospital sector, hospital purchases from wholesalers (tenders and self-procurement) and pharmacy purchases from wholesalers. Retail and hospital estimates are based on extrapolation of representative sample data using cluster analysis and hierarchical models. Tender data are derived from official information from the ProZorro platform.

In some cases, data are not available for all years examined.

2.1.2 Data collection

Data collection is based on a standardized protocol that is aligned with the WHO methodology for a global programme on surveillance of antimicrobial consumption (WHO, 2017b). Data are collected at the product level (proprietary and generic products) and comprise information on the active substance(s) of the product, route of administration, strength per unit, number of units per package and total number of packages consumed. Data collection is facilitated by means of a standard Excel template with functions to calculate volume and consumption for each product. Further details on the template for data collection are available in previous AMC Network reports (WHO Regional Office for Europe 2017, 2020, 2021).

2.2 ATC and DDD classification systems

Like the WHO global methodology, the AMC Network uses the ATC classification system to distinguish between pharmacological subgroups and substance levels of antimicrobials, and uses DDD as the primary measurement metric (WHO Collaborating Centre for Drug Statistics Methodology, 2020).

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 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 used only 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.

2.3 Antibacterial agents included in this report

The main analyses presented here are for the antibacterials for systemic use (ATC group J01) and related pharmacological subgroups. Data on additional antimicrobials are included in the calculation of the 2021 WHO AWaRe classification (WHO, 2021), namely neomycin (A07AA01), streptomycin oral (A07AA04), polymyxin B oral (A07AA05), kanamycin oral (A07AA08), vancomycin oral (A07AA09), colistin oral (A07AA10), rifamixin (A07AA11), fidaxomicin (A07AA12), rifamycin oral (A07AA13), rifampicin (J04AB02), rifamycin intravenous (J04AB03), rifabutin (J04AB04), metronidazole oral (P01AB01), tinidazole oral (P01AB02), ornidazole oral (P01AB03) and secnidazole (P01AB07) (Table 2.2).

Additions new to the 2021 AWaRe index (beyond those included in the J01 category) are fidaxomicin (Watch), ornidazole oral (Access), rifamycin oral (Watch), secnidazole (Access) and tinidazole oral (Access). None of these agents is listed on the WHO Model List of Essential Medicines for adults/children (EML/EMLc) 2021 (WHO, 2021).

Table 2.2 Antibacterials included in the analyses

Class of agents	ATC code (medicine)
Antibacterials for systemic use	J01
Pharmacological subgroups of J01	
Tetracyclines	J01A
Amphenicols	J01B
Beta-lactam antibacterials, penicillins	J01C
Other beta-lactam antibacterials	J01D
Sulfonamides and trimethoprim	J01E
Macrolides, lincosamides and streptogramins	J01F
Aminoglycoside antibacterials	J01G
Quinolone antibacterials	J01M
Combinations of antibacterials	J01R
Other antibacterials	J01X
Antibiotics for intestinal tract	A07AA01 (neomycin) A07AA04 (streptomycin) A07AA05 (polymyxin B) A07AA08 (kanamycin) A07AA09 (vancomycin) A07AA10 (colistin) A07AA11 (rifaximin) A07AA12 (fidaxomicin) A07AA13 (rifamycin oral)
Antimycobacterials	J04AB02 (rifampicin) J04AB03 (rifamycin) J04AB04 (rifabutin)
Nitroimidazole derivatives	P01AB01 (metronidazole) P01AB02 (tinidazole) P01AB03 (ornidazole) P01AB07 (secnidazole)

ATC: Anatomical Therapeutic Chemical (classification system).

2.4 Metrics and indicators reported

2.4.1 Measures of volume and relative consumption

Total numbers of DDDs for each product are aggregated to give the total number of DDDs at the desired ATC code level. The number of DDDs provides a measure of the 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 disaggregation of data that is possible. For most antibacterials, DDD per 1000 inhabitants per day (DID) are calculated for the total population, including all age and gender groups.

World Bank population estimates (World Bank, 2020) were applied to most AMC Network countries/areas apart from Türkiye, where estimates were adjusted to take account of the large refugee population, and North Macedonia and Switzerland, where national population estimates were used.

Patterns of consumption in 2018 by ATC level 3 subgroups of J01 antibacterial agents and by route of administration (oral and parenteral) were assessed. Both volumes in DID and measures of relative consumption, expressed as a percentage of total consumption of groups of antimicrobials, were derived for pharmacological subgroups of J01.

2.4.1.1 Total consumption in DID

The DID is the primary indicator of antibiotic consumption in countries/areas as defined by the European Commission and WHO (European Centre for Disease Prevention and Control et al., 2017) and is a key indicator reported in the first WHO global report on antimicrobial consumption (WHO, 2018).

It should be noted that only medicines with an assigned ATC code and DDD are included in the analyses reported here. In several countries in the AMC Network, several 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.

2.4.1.2 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 safely be 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. It nevertheless 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 consumption of parenteral formulations is comparatively high, there may be opportunities to increase use of oral formulations without loss of clinical efficacy.

2.4.1.3 Consumption of pharmacological subgroups (ATC3 level)

Absolute and relative consumption figures for pharmacological subgroups of J01 (ATC3 level) are presented in this report.

2.4.2 Trends in total consumption over time

To illustrate changes in rates in antimicrobial consumption over time, the compound annual growth rate (CAGR) of total antibiotic consumption was calculated for each participating country. This reflects the average annual change as a proportion (%) of the consumption in the starting year. CAGRs were estimated for countries that had five years of data available.

Linear regression was used for presenting trends in consumption for each participating country/area and evaluated using analysis of variance (ANOVA) tests. P values ≤ 0.05 were considered statistically significant.

2.4.3 WHO AWaRe classification

In April 2017, the WHO Expert Committee on the Selection and Use of Essential Medicines proposed a categorization of antibiotics into Access, Watch and Reserve groups. Not all medicines on the model lists were assigned to the three groups, leaving a fourth "unclassified" category, with the classification to be revised as additional clinical syndromes are reviewed. The characteristics of these groups are shown in Table 2.3. A detailed description of the origins of the WHO AWaRe classification is available in the WHO global report on antimicrobial consumption (WHO, 2018).

In 2019, the AWaRe classification was expanded beyond the antibiotics listed on the EML and EMLc (WHO, 2019a, 2019b). As a result, 180 antibiotics used globally were assigned to either Access (n = 48), Watch (n = 110) or Reserve (n = 22) groups. In addition to classifying 180 antibiotics, WHO created a list of 103 antibiotics that are not recommended – fixed-dose combinations of multiple broad-spectrum antibiotics that lack evidence-based indications for use or recommendations in high-quality international guidelines. WHO suggests that the use of these antibiotics should be actively discouraged.

In 2021, the AWaRe classification was again refined. The Expert Committee endorsed the recommendations of the EML Antibiotics Working Group for the addition of 81 antibiotics to the index – 40 as Access, 34 as Watch and 7 as Reserve agents (WHO, 2021). Several of the new additions are different formulations of agents already included in the AWaRe index, for example the addition of oral formulations of colistin, neomycin, polymyxin B and rifamycin. The agents listed in the 2021 AWaRe index are shown in the Annex.

Table 2.3 WHO categories of antibiotics – descriptions

Group	Definition
Access agents	This group includes antibiotics that have activity against a wide range of commonly encountered susceptible pathogens while also showing lower resistance potential than antibiotics in the other groups.
Watch agents	This group includes antibiotics that have higher resistance potential and includes most of the highest priority agents among the Critically Important Antimicrobials for Human Medicine and/or antibiotics that are at relatively high risk of selection of bacterial resistance. Antibiotics in the Watch group should be prioritized as key targets of stewardship programmes and monitoring.
Reserve agents	This group includes antibiotics and antibiotic classes that should be reserved for treatment of confirmed or suspected infections due to multidrug-resistant organisms. Antibiotics in the Reserve group should be treated as "last resort" options; they should be accessible, but their use should be tailored to highly specific patients and settings when all alternatives have failed or are not suitable. These medicines could be protected and prioritized as key targets of national and international stewardship programmes involving monitoring and utilization reporting to preserve their effectiveness.
Unclassified	These are medicines not specifically identified in the groups described above. Some unclassified agents are included in WHO's list of "not recommended antibiotics". The "not recommended" agents are the fixed-dose combinations of multiple broad-spectrum antibiotics whose use is neither evidence-based nor recommended in high-quality international guidelines. WHO does not recommend their use in clinical practice.

The AWaRe classification can be used to inform stewardship activities both in community and hospital sectors. The proportions of consumption (%) according to the AWaRe classification are presented in this report.

It is not possible to assess levels of use of "not recommended" antibiotics, as these combination medicines do not always have an assigned ATC code and therefore are not included in data collection.

2.4.4 WHO global monitoring indicator

In conjunction with the expansion of the list of antibiotics included in the AWaRe classification, WHO has proposed a global monitoring indicator that by 2023, 60% of all antibiotics consumed should come from Access, the group of antibiotics at lowest risk of resistance (WHO, 2019c).

The proportion of total consumption that comprised Access agents was calculated for each year of analysis from 2014 to 2019. The number of countries reaching the WHO global monitoring target in 2019 and across each of the years assessed is reported.

2.4.5 Access-to-Watch indicator

This indicator has been used in several published papers (Hsia et al., 2019; Klein et al., 2020). The measure is calculated as the ratio of DDDs of Access medicines to DDDs of Watch medicines.

The highest Access-to-Watch index scores will be reported in countries/areas with the highest proportional consumption of Access antibacterials. If only Access and Watch agents were consumed, then consumption of 60% Access agents and 40% Watch agents would give a ratio of 1.5:1.

2.4.6 DU75%

In the 2017 and 2020 AMC Network reports, the 10 most consumed oral formulations and 10 most consumed parenteral formulations were presented. These analyses are based on the observations of ESAC-Net and other analyses that consumption tends to be concentrated in a relatively small number of agents.

In the 2021 AMC Network report, the DU75% was calculated. This metric was considered in the WHO global report on antimicrobial consumption (WHO, 2018), where results were stratified by route of administration (oral and parenteral formulations) and reported by region. All substances that appeared on the DU75% lists in countries/areas within a region were compiled into a region-specific list for oral substances and parenteral substances, respectively.

The DU75% for 2018 was reported by country/area and across networks in the 2021 joint publication on AMC data from ESAC-Net and the WHO Regional Office for Europe (Robertson et al., 2021).

In this report, the DU75% is calculated for oral and parenteral formulations separately. Results are shown as the ranking of consumption at substance level (fifth ATC group level), volumes in DID and percentages of total consumption. In addition to reporting the numbers of antibacterial agents in the DU75% segment, this report categorizes the agents in this segment according to the AWaRe classification. This facilitates identification of restricted and special use antibacterials that may be consumed widely and be potential targets for stewardship activities.

2.4.7 Summary measures applied to cross-national comparisons

AMC Network summary data are presented using arithmetic and population-weighted mean estimates.

Arithmetic means for total consumption are derived by summing the national estimates for total consumption and dividing by the number of countries contributing data to the calculation.

Population-weighted estimates for total consumption are calculated by multiplying DDD per 1000 inhabitants per day for each country with the corresponding population, summing the country estimates and dividing the total DDDs by the total population of participating countries (European Centre for Disease Prevention and Control, 2019).

Using similar methods, population-weighted estimates are calculated for the relative consumption of Access, Watch and Reserve group agents and for components of the DU75% in the AMC Network.

2.4.8 Metrics reported in the analyses

The key metrics used in analyses and included in this report are summarized in Table 2.4.

Table 2.4 Metrics used in analyses and included in this report

Category	Unit
Estimates of volumes of consumption of antibacterials for systemic use (J01)	
Total consumption of J01 antibacterials by route of administration	DID
Total consumption of J01 antibacterials by pharmacological subgroup (ATC3): - tetracyclines (J01A) - amphenicols (J01B) - beta-lactam antibacterials, penicillins (J01C) - other beta-lactams (includes 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	%
Relative consumption of WHO Access, Watch, Reserve antibiotics[a]	
Relative consumption of Access, Watch and Reserve group agents	%
Access-to-Watch index	Ratio
Concordance with WHO global monitoring indicator	
Proportion of total consumption that is Access agents	%
DU75%	
DU75% – oral formulation	Rank, DID, %
DU75% – parenteral formulation	Rank, DID, %
Summary metrics reported in cross-national comparisons	
Arithmetic mean estimates of: - total consumption of J01 antibacterials - consumption of pharmacological subgroups (ATC3 level) - consumption of agents according to AWaRe classification	 DID DID, % DID, %
Population-weighted mean estimates of: - total consumption of J01 antibacterials - consumption of pharmacological subgroups (ATC3 level) - consumption of agents according to AWaRe classification - agents comprising the DU75%	 DID DID, % % Rank

ATC: Anatomical Therapeutic Chemical (classification system); DID: defined daily doses per 1000 inhabitants per day; DU75%: antibacterial substances accounting for 75% of consumption.
[a] Total consumption of antibiotics for this calculation includes: J01 antibacterials, neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), fidaxomicin (A07AA12), rifamycin oral (A07AA13), rifampicin (J04AB02), rifamycin intravenous (J04AB03), rifabutin (J04AB04), metronidazole (P01AB01), tinidazole (P01AB02), ornidazole (P01AB03) and secnidazole (P01AB07).

Joint interpretation of these metrics will help to identify broad areas for national antibiotic stewardship and guideline development, even when information about indication is not available. Previous AMC Network reports have described several limitations to the data sources used. Even with these limitations, the variability of consumption patterns within and between countries/areas 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 access), data sources, resistance patterns and the potential impact of interventions to change practices.

3. COMPARISON OF 2019 ANTIMICROBIAL MEDICINES CONSUMPTION ACROSS THE AMC NETWORK

In this chapter, comparisons are conducted across 14 AMC Network members providing 2019 consumption data. Where possible, comparisons with 2018 are provided.

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

3.1.1 Total consumption

Total consumption of antibacterials for systemic use (ATC class J01) is examined by route of administration (oral and parenteral formulations) (Fig. 3.1 and Table 3.1).

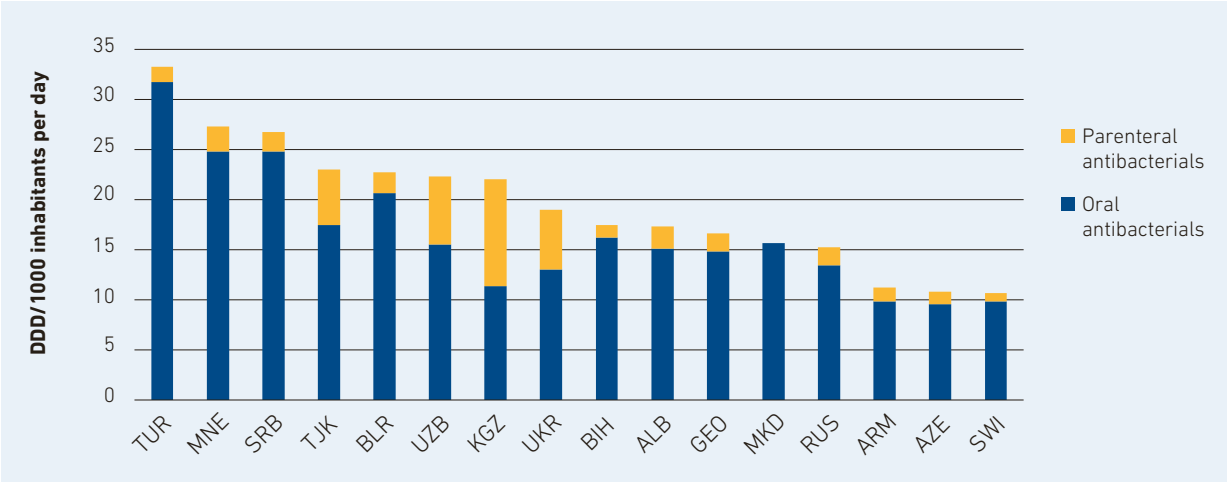
Consistent with previous analyses of AMC Network data, there is wide variability in reported consumption of J01 antibacterials – ranging from 33.2 DID (Türkiye) to 10.6 DID (Switzerland). This compares to a range of 30.9 DID (Türkiye) to 8.9 DID (Azerbaijan) in 2018.

The median consumption in 2019 was 19.6 DID (18.8 DID using 2018 data across 17 network members). The arithmetic and population-weighted mean totals of J01 consumption in 2019 were 19.6 and 21.2 DID, respectively (compared to 17.5 and 18.5 DID in 2018).

3.1.2 Route of administration

The extent of consumption of parenteral formulations varied widely, from 5% in Türkiye up to 49% in Kyrgyzstan (Table 3.1). The range in 2018 was 3% (Türkiye) to 40% (Kyrgyzstan). Data for North Macedonia relate to community consumption of oral antibiotics only.

Fig. 3.1 Total consumption of J01 antibacterials by route of administration in 2019



DDD: daily defined dose.

Table 3.1 Total consumption of J01 antibacterials by route of administration, 2019

Route of administration	DDD/1000 inhabitants per day (% of total[a])														
	TUR	MNE	SRB	TJK	BLR	UZB	KGZ	BIH	GEO	MKD	RUS	ARM	AZE	SWI	WHO/AMC [b]
Oral J01	31.5 (95)	24.7 (91)	24.7 (93)	17.4 (76)	20.5 (91)	15.5 (70)	11.3 (51)	16.1 (92)	14.7 (89)	15.6 (100)	13.3 (87)	9.7 (87)	9.5 (89)	9.8 (92)	18.7 (88)
Parenteral J01	1.6 (5)	2.4 (9)	1.8 (7)	5.5 (24)	2.0 (9)	6.7 (30)	10.6 (49)	1.3 (8)	1.8 (11)	–	1.9 (13)	1.5 (13)	1.2 (11)	0.8 (8)	2.5 (12)
Total[a]	**33.2**	**27.1**	**26.6**	**22.8**	**22.6**	**22.2**	**21.9**	**17.4**	**16.5**	**15.6**	**15.2**	**11.2**	**10.8**	**10.6**	**21.2**

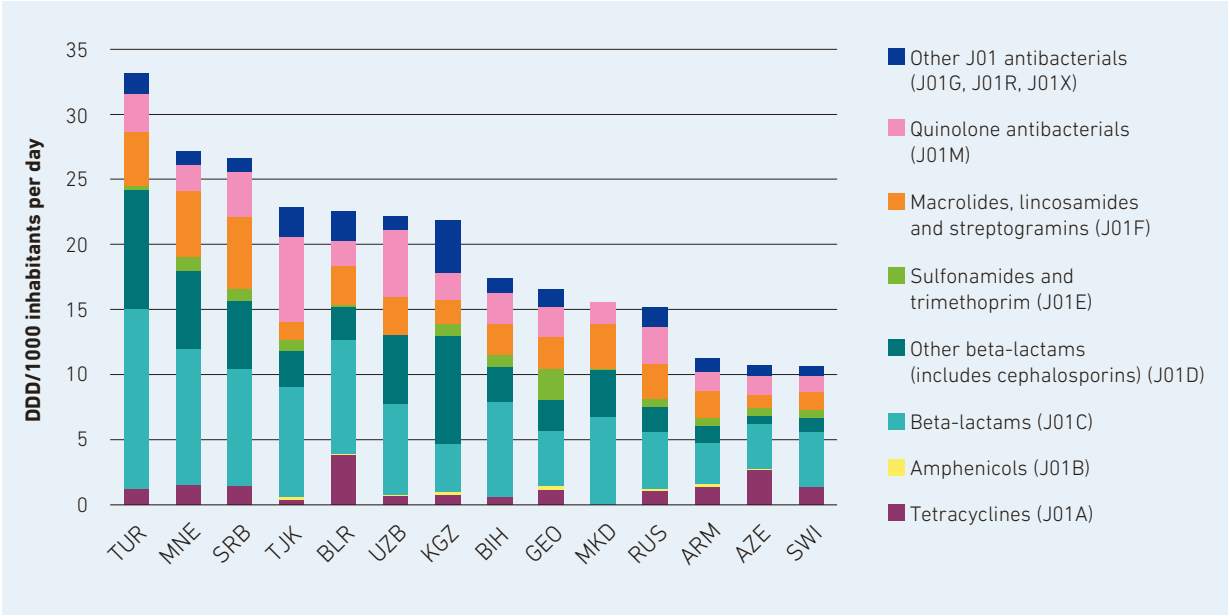
DDD: daily defined dose.
[a] Total amounts and percentages may vary slightly due to rounding. [b] WHO/AMC population-weighted mean for countries of the AMC Network.

3.1.3 Pharmacological subgroups

Total consumption of antibacterials for systemic use (ATC class J01) is examined by pharmacological subgroup (Fig. 3.2 and Table 3.2).

There was considerable variation in the extent of consumption of the different pharmacological subgroups across the AMC Network. In 2019, consumption of beta-lactam penicillins (J01C) ranged from 17% of total J01 consumption in Kyrgyzstan to 42% of J01 consumption in Bosnia and Herzegovina and Türkiye, and 43% in North Macedonia (Table 3.2). Cephalosporin (J01D) consumption varied from 6% of J01 consumption in Azerbaijan to 38% in Kyrgyzstan. Quinolone (J01M) consumption varied from 7% in Montenegro to 28% in Tajikistan.

Fig. 3.2 Total consumption of J01 antibacterials by pharmacological subgroup, 2019



DDD: daily defined dose.

Table 3.2 Total consumption of J01 antibacterials by pharmacological subgroup, 2019

Class of antibacterial agents	DDD/1000 inhabitants per day (% of total[a])														
	TUR	MNE	SRB	TJK	BLR	UZB	KGZ	BIH	GEO	MKD	RUS	ARM	AZE	SWI	WHO/AMC [b]
Tetracyclines (J01A)	1.3 (4)	1.5 (6)	1.5 (6)	0.5 (2)	3.9 (17)	0.7 (3)	0.8 (4)	0.6 (4)	1.2 (7)	<0.1 (0)	1.1 (7)	1.4 (12)	2.7 (25)	1.3 (13)	1.2 (6)
Amphenicols (J01B)	–	–	–	0.2 (1)	0.1 (0)	0.1 (1)	0.2 (1)	–	0.2 (1)	–	0.2 (1)	0.3 (3)	0.1 (1)	–	0.1 (0)
Beta-lactam penicillins (J01C)	13.7 (42)	10.5 (39)	9.0 (34)	8.4 (37)	8.7 (39)	7.0 (31)	3.7 (17)	7.3 (42)	4.2 (26)	6.7 (43)	4.4 (29)	3.1 (27)	3.5 (32)	4.3 (40)	7.5 (35)
Other beta-lactams (includes cephalosporins) (J01D)	9.2 (28)	6.0 (22)	5.1 (19)	2.8 (12)	2.5 (11)	5.3 (24)	8.3 (38)	2.7 (16)	2.4 (15)	3.6 (23)	1.9 (12)	1.4 (12)	0.6 (6)	1.1 (10)	4.4 (21)
Sulfonamides and trimethoprim (J01E)	0.3 (1)	1.0 (4)	0.9 (4)	0.8 (4)	0.1 (1)	–	0.9 (4)	0.9 (5)	2.3 (14)	0.1 (1)	0.6 (4)	0.6 (5)	0.6 (6)	0.6 (5)	0.5 (2)
Macrolides, lincosamides and streptogramins (J01F)	4.1 (12)	5.1 (19)	5.6 (21)	1.4 (6)	3.1 (14)	3.0 (13)	1.8 (8)	2.4 (14)	2.4 (15)	3.4 (22)	2.7 (18)	2.1 (19)	1.0 (10)	1.4 (13)	3.0 (14)
Quinolone antibacterials (J01M)	3.0 (9)	2.0 (7)	3.5 (13)	6.5 (28)	1.9 (8)	5.1 (23)	2.1 (10)	2.4 (14)	2.3 (14)	1.7 (11)	2.9 (19)	1.4 (13)	1.5 (14)	1.2 (12)	3.1 (14)
Other J01 antibacterials (J01G, J01R, J01X)	1.6 (5)	1.0 (4)	1.0 (4)	2.2 (10)	2.3 (10)	1.1 (5)	4.0 (19)	1.1 (6)	1.4 (8)	–	1.5 (10)	1.0 (9)	0.8 (8)	0.7 (7)	1.5 (7)
Total	**33.2**	**27.1**	**26.6**	**22.8**	**22.6**	**22.2**	**21.9**	**17.4**	**16.5**	**15.6**	**15.2**	**11.2**	**10.8**	**10.6**	**21.2**

DDD: daily defined dose.
[a] Total amounts and percentages may vary slightly due to rounding. [b] WHO/AMC population-weighted mean for countries of the AMC Network.

3.1.4 Trends, 2014–2019

Table 3.3 shows the trends in total consumption of antibacterials for systemic use (ATC J01) for the years 2014–2019. The CAGR of total antibiotic consumption was calculated for each participating country. This reflects the average annual change as a proportion (%) of the consumption in the starting year. The CAGR was estimated for countries that had five years of data available. Linear regression was used for presenting trends in consumption and evaluated using ANOVA tests. P values ≤ 0.05 were considered statistically significant.

There were statistically significant increases in total consumption between 2014 and 2019 in two countries, namely Azerbaijan (+13.8%) and Russian Federation (+3.2%) (Table 3.3).

Table 3.3 Trends in consumption of J01 antibacterials, 2014–2019

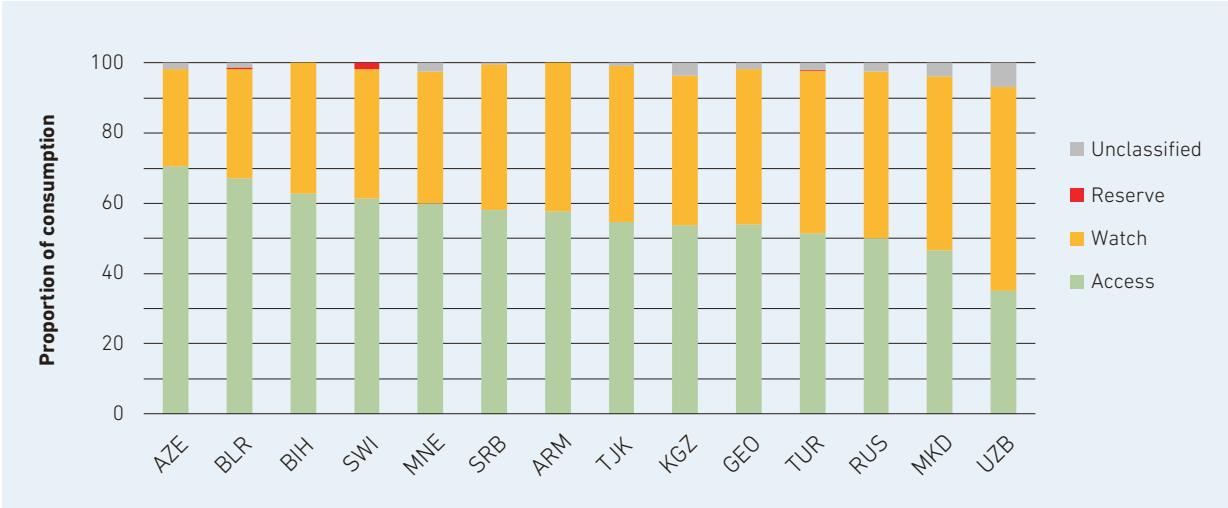
Country	Total consumption of J01 antibacterials in DDD/1000 inhabitants per day						CAGR[a]	Trend line, 2014–2019	Trend[b]
	2014	2015	2016	2017	2018	2019			
ALB	19.6	16.3	16.5	18.7	19.0	–	-0.7%	–	
ARM	12.7	9.4	9.4	12.0	12.1	11.2	-3.2%		
AZE	6.4	7.4	9.5	7.8	8.9	10.8	13.8%		↑
BIH	15.3	16.3	18.0	17.4	19.3	17.4	3.2%		
BLR	18.3	17.1	16.9	20.0	18.9	22.6	5.4%		
GEO	17.9	24.2	23.6	25.1	20.8	16.5	-2.0%		
KAZ	–	17.4	15.7	14.3	15.1	–	–	–	
KGZ	–	16.7	21.3	16.9	11.2	21.9	–	–	
MDA	16.7	12.9	16.7	17.1	14.2	–	-4.1%	–	
MKD	16.3	16.7	17.0	16.9	16.6	15.6	-1.1%		
MNE	26.7	29.0	28.9	27.1	27.0	27.1	0.4%		
RUS	13.4	14.1	14.9	15.1	14.7	15.2	3.2%		↑
SRB	25.3	31.0	26.2	21.3	22.7	26.6	1.2%		
SWI	–	–	–	10.4	10.6	10.6	–	–	
TJK	31.0	21.7	20.9	16.3	19.0	22.8	-7.4%		
TUR	34.7	35.5	35.3	31.0	30.9	33.2	-1.2%		
UKR	9.5	12.1	8.3	10.7	11.7	–	5.3%	–	
UZB	–	–	25.1	16.3	18.2	22.2	–	–	

CAGR = compound average growth rate.
[a] The CAGR was only calculated where there was five years of data (2014–2018) available for the country. [b] Linear regression analysis.
↑↓ indicates statistically significant change.

3.2 Relative consumption of Access, Watch and Reserve groups of antibiotics

Analyses based on the 2021 WHO Access, Watch and Reserve groups of antibiotics can support antimicrobial stewardship efforts and focus attention on prescribing practices that should be reviewed further. The relative consumption of Access, Watch and Reserve group antibiotics is shown in Fig. 3.3 and is summarized in Table 3.4.

Fig. 3.3 Relative consumption by WHO AWaRe classification as a proportion of total consumption[a,b], 2019



[a] Countries are presented in order of their consumption of Access agents, from highest to lowest percentage. [b] Total consumption of antibiotics for this calculation includes J01 antibacterials, neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), fidaxomicin (A07AA12), rifamycin oral (A07AA13), rifampicin (J04AB02), rifamycin intravenous (J04AB03), rifabutin (J04AB04), metronidazole (P01AB01), tinidazole (P01AB02), ornidazole (P01AB03) and secnidazole (P01AB07).

Consumption of Access agents represented between 35% (Uzbekistan) and 71% (Azerbaijan) of total antibacterial consumption in 2019 (Table 3.4). In 12 of 14 countries (86%), Access agents comprised ≥ 50% of total antibacterial consumption.

Watch group agents represented between 28% (Azerbaijan) and 58% (Uzbekistan) of total consumption. Consumption of Reserve agents remained low in all 14 countries. Unclassified agents constituted 4% of consumption in North Macedonia and 7% of consumption in Uzbekistan.

The 2019 population-weighted estimates across the AMC Network were: Access agents 50.6%, Watch agents 46.7%, Reserve agents 0.2% and unclassified agents 2.5%. The comparable estimates across 17 network countries in 2018 were: Access agents 46.9%, Watch agents 49.5%, Reserve agents 0.1% and unclassified agents 3.5%.

Table 3.4 Relative consumption of Access, Watch and Reserve classification antibacterials, 2019[a]

Group of antibacterial agents	DDD/1000 inhabitants per day (% of total)														
	Consumption according to 2019 WHO AWaRe classification[b]														
	AZE	BLR	BIH	SWI	MNE	SRB	ARM	TJK	KGZ	GEO	TUR	RUS	MKD	UZB	WHO/AMC[c]
Access	7.9 (71%)	15.7 (67%)	11.1 (63%)	6.8 (61%)	16.6 (60%)	15.9 (58%)	6.7 (57%)	12.7 (55%)	12.2 (54%)	9.0 (54%)	17.9 (51%)	8.0 (50%)	7.3 (46%)	7.8 (35%)	11.2 (51%)
Watch	3.1 (28%)	7.3 (31%)	6.6 (37%)	4.1 (37%)	10.4 (38%)	11.4 (41%)	4.9 (42%)	10.3 (44%)	9.7 (43%)	7.4 (44%)	16.1 (46%)	7.6 (47%)	7.8 (50%)	12.9 (58%)	10.3 (47%)
Reserve	–	0.1 (0%)	<0.1 (0%)	0.2 (1%)	<0.1 (0%)	<0.1 (0%)	<0.1 (0%)	<0.1 (0%)	–	<0.1 (0%)	0.1 (0%)	<0.1 (0%)	–	<0.1 (0%)	<0.1 (0%)
Unclassified	0.2 (2%)	0.3 (1%)	<0.1 (0%)	<0.1 (0%)	0.7 (3%)	0.1 (1%)	<0.1 (0%)	0.2 (1%)	0.8 (3%)	0.3 (2%)	0.7 (2%)	0.4 (2%)	0.6 (4%)	1.5 (7%)	0.6 (3%)
Total	**11.2**	**23.3**	**17.8**	**11.1**	**27.7**	**27.4**	**11.7**	**23.2**	**22.7**	**16.7**	**34.7**	**16.0**	**15.7**	**22.2**	**22.1**

[a] Countries are presented in order of their consumption of Access agents, from highest to lowest percentage. [b] Total consumption of antibiotics for this calculation includes: J01 antibacterials, neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), fidaxomicin (A07AA12), rifamycin oral (A07AA13), rifampicin (J04AB02), rifamycin intravenous (J04AB03), rifabutin (J04AB04), metronidazole (P01AB01), tinidazole (P01AB02), ornidazole (P01AB03) and secnidazole (P01AB07). [c] Total amounts and percentages may vary slightly due to rounding.

3.2.1 WHO global monitoring indicator

In conjunction with the expansion of the list of antibiotics included in the AWaRe classification in 2019, WHO proposed a global monitoring indicator that by 2023, 60% of all antibiotics consumed should come from Access, the group of antibiotics at lowest risk of resistance (WHO, 2019c).

Five countries (Azerbaijan, Belarus, Bosnia and Herzegovina, Montenegro and Switzerland) would have met the WHO target of at least 60% of total consumption being Access agents in 2019 (Table 3.5). This is a slight change from 2018 estimates, where four countries (Azerbaijan, Armenia, Bosnia and Herzegovina, and Switzerland) would have met the WHO target.

Trends in the relative consumption of Access agents in 2014–2019 are shown in Table 3.5. Only one country in the AMC Network would have met the global monitoring indicator in each of the six years examined – Bosnia and Herzegovina.

Table 3.5 Countries achieving target of 60% of total consumption being Access agents, 2014–2019

Country[a]	Access agents as proportion (%) of total consumption[b]					
	2014	2015	2016	2017	2018	2019
ALB	61	48	51	44	40	–
ARM	67	68	57	66	63	57
AZE	58	61	50	56	62	71
BIH	69	69	70	68	66	63
BLR	57	60	56	62	61	67
GEO	32	46	60	64	43	54
KAZ	–	63	60	57	53	–
KGZ	–	72	56	50	34	54
MDA	49	56	47	49	51	–
MKD	53	49	50	48	47	46
MNE	61	56	58	59	57	60
RUS	51	51	51	51	50	50
SRB	68	65	63	60	51	58
SWI	–	–	–	58	60	61
TJK	65	58	62	46	43	55
TUR	45	45	47	48	51	51
UKR	46	37	51	42	40	–
UZB	–	–	31	42	30	35

Note: Green cells indicate that a country has met the 60% target.
[a] Country estimates are rounded up. [b] Total consumption of antibiotics for this calculation includes: J01 antibacterials, neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), fidaxomicin (A07AA12), rifamycin oral (A07AA13), rifampicin (J04AB02), rifamycin intravenous (J04AB03), rifabutin (J04AB04), metronidazole (P01AB01), tinidazole (P01AB02), ornidazole (P01AB03) and secnidazole (P01AB07).

3.2.2 Unclassified agents

As part of the 2019 revision of the AWaRe classification, WHO created a list of 103 antibiotics that are not recommended. These are mostly fixed-dose combinations of multiple broad-spectrum antibiotics that lack evidence-based indications for use or recommendations in high-quality international guidelines. The use of these antibiotics should be actively discouraged. Several agents that are consumed in the AMC Network are yet to be assigned the AWaRe classification.

Table 3.6 summarizes the unclassified agents, including "not recommended agents", and their consumption volumes in 2019. Not all agents included in the "not recommended" list have an ATC code or DDD assigned. The volumes of use of these agents will not be captured in Table 3.6.

Table 3.6 Unclassified and "not recommended" agents consumed in AMC Network, 2019

ATC	Agent	DDD/1000 inhabitants/day												
		ARM	AZE	BIH	BLR	GEO	KGZ	MKD	MNE	RUS	SRB	TJK	TUR	UZB
A07AA02	Nystatin	0.34	0.35	0.10	0.20	–	–	0.04	0.50	0.31	0.23	0.30	0.13	–
A07AA03	Natamycin	0.02	< 0.01	–	0.01	–	–	–	–	0.06	–	< 0.01	–	–
J01CE10	Benzathine phenoxymethylpenicillin	–	–	–	–	–	–	0.60	0.61	–	–	–	0.29	–
J01CE30	Combinations[a]	0.01	< 0.01	0.04	0.02	0.03	–	–	0.09	0.01	0.07	0.01	0.01	–
J01XX05	Methenamine	–	–	–	–	–	–	–	–	–	–	–	0.35	–
J01XX07	Nitroxoline	0.04	0.20	–	0.12	0.16	0.25		0.02	0.19	0.07	0.06	–	–
P01AB06	Nimorazole	< 0.01	–	–	–	–	–	–	–	< 0.01	–	–	–	–
J01DD62	Cefoperazone and beta-lactamase inhibitor[b]	–	–	–	–	0.01	–	–	–	0.02	–	< 0.01	0.01	0.07
J01DD63	Ceftriaxone and beta-lactamase inhibitor[c]	–	–	–	–	–	0.03	–	–	–	–	0.03	–	0.21
J01DD64	Cefpodoxime and beta-lactamase inhibitor[d]	–	–	–	–	–	–	–	–	–	–	–	< 0.01	–
Antibiotics not recommended														
J01RA05	Levofloxacin and ornidazole	–	–	–	–	–	–	–	–	–	–	0.01	–	–
J01RA07	Azithromycin, fluconazole and secnidazole	–	–	–	–	< 0.01	–	–	–	< 0.01	–	< 0.01	–	–
J01RA09	Ofloxacin and ornidazole	–	–	–	–	–	0.02	–	–	0.01	–	–	–	0.07
J01RA11	Ciprofloxacin and tinidazole	–	–	–	0.12	–	0.25	–	–	0.16	–	0.02	–	0.03
J01RA12	Ciprofloxacin and ornidazole	–	–	–	–	0.11	–	–	–	–	–	0.02	< 0.01	0.01
J01RA13	Norfloxacin and tinidazole	–	–	–	–	–	0.20	–	–	–	–	–	–	0.12

ATC: Anatomical Therapeutic Chemical (classification system); DDD: daily defined dose.
Data for Switzerland are not available.
[a] Combinations of benzylpenicillin and procaine penicillin. [b] Combinations of cefoperazone/sulbactam and cefoperazone/tazobactam are specified in WHO's "not recommended" list of antibiotics. [c] Combinations of ceftriaxone/sulbactam and ceftriaxone/tazobactam are specified in WHO's "not recommended" list of antibiotics. [d] Combinations of cefpodoxime proxetil/clavulanic acid and cefpodoxime proxetil/sulbactam are specified in WHO's "not recommended" list of antibiotics.

The most widely consumed unclassified agents from the J01 class in the AMC Network in 2019 were combinations of benzylpenicillin and procaine penicillin (J01CE30) consumed in 10 of the 14 countries, and nitroxoline (J01XX07) in 9 countries.

Furazidin (J01XE03) use was reported in 10 countries in 2018 estimates, however this J01 agent has now been classified as an Access agent.

Several "not recommended" combinations of antibacterials were consumed in AMC Network countries in 2019, including ciprofloxacin and tinidazole (J01RA11, five countries); ciprofloxacin and ornidazole (J01RA12, four countries); ofloxacin and ornidazole (J01RA09, three countries); azithromycin, fluconazole and secnidazole (J01RA07, three countries); and norfloxacin and tinidazole (two countries). These "not recommended" combination products are potential targets for further investigation and local interventions to discourage their use in clinical practice.

3.2.3 Access-to-Watch index

This indicator has been used in several published papers (Hsia et al., 2019; Klein et al., 2020). The measure is calculated as the ratio of DDDs of Access medicines to DDDs of Watch medicines. The results of this analysis are shown in Table 3.7.

Table 3.7 Access-to-Watch index, 2019

Country	AZE	BLR	BIH	SWI	MNE	SRB	ARM	TJK	GEO	KGZ	TUR	RUS	MKD	UZB
Access-to-Watch index score[ab]	2.49	2.02	1.69	1.64	1.61	1.42	1.33	1.23	1.21	1.24	1.08	1.00	0.94	0.60

[a] Ratio of the consumption of Access-to-Watch antibiotics. [b] Antibiotics for this calculation include: J01 antibacterials, neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), fidaxomicin (A07AA12), rifamycin oral (A07AA13), rifampicin (J04AB02), rifamycin intravenous (J04AB03), rifabutin (J04AB04), metronidazole (P01AB01), tinidazole (P01AB02), ornidazole (P01AB03) and secnidazole (P01AB07).

A ratio of 1.5 would be consistent with a distribution of Access-to-Watch agents of 60% to 40%. Only five countries had ratios ≥ 1.5. Lower ratios (< 1.5) reflect higher relative consumption of Watch agents.

3.3 DU75%

The DU75% represents the antibacterial substances accounting for 75% of consumption measured in DDD (Zarb et al., 2011). The DU75% is calculated for oral and parenteral formulations separately. Results are shown as the ranking of consumption at substance level (fifth ATC group level). In addition to reporting the numbers of antibacterial agents in the DU75% segment, the agents are categorized according the AWaRe classification. This facilitates identification of restricted and special use antibacterials that may be widely consumed and be potential targets for stewardship activities.

Table 3.8 (oral agents) and Table 3.9 (parenteral agents) show the ranking of consumption of antibacterial agents that comprise the DU75%.

In 2019, the number of agents constituting the DU75% by oral substance ranged from 5 to 10 across the AMC Network countries (Table 3.8). There were 10 agents in the population-weighted DU75% for the AMC Network.

Oral amoxicillin and beta-lactamase inhibitor (ATC code J01CR02) was included in the DU75% in 13 of 14 Network countries, ranked first for consumption in five of those countries and first in the population-weighted DU75%. Amoxicillin (J01CA04) ranked second in the population-weighted DU75%, appeared in the DU75% for 12 countries, and was ranked the most consumed oral antibiotic in eight countries.

Ciprofloxacin (J01MA02), a fluoroquinolone, was included in the DU75% for 12 of the 14 Network countries and was ranked first to sixth most consumed antibiotic in those countries. It ranked third in the population-weighted DU75%.

Azithromycin (J01FA10), a macrolide, was included in the DU75% for 13 of the 14 Network countries and was ranked second to eighth most consumed antibiotic in those countries. It ranked fourth in the population-weighted DU75%.

Two to six Watch agents appeared in the DU75% for each of the AMC Network countries and there were six Watch agents in the population-weighted network estimate.

There were no unclassified oral agents included in the DU75% for any AMC Network country.

In 2019, the number of agents constituting the DU75% by parenteral substance ranged from 3 to 10 across the AMC Network countries (Table 3.9). There were nine agents in the population-weighted DU75%.

The Watch agent ceftriaxone (J01DD04) was ranked number one in nine countries and ranked second in three countries.

3.4 Other monitoring indicators

ESAC-Net quality indicators for antibiotic consumption in the community include a measure of the relative use of narrow- and broad-spectrum antibiotics within J01 group antibiotics (European Centre for Disease Prevention and Control, 2020). The indicator is calculated as the ratio between the consumption of broad-spectrum antibiotics (J01CR, J01DC, J01DD and J01F (without erythromycin)) and narrow-spectrum penicillins, cephalosporins and macrolides (J01CE, J01DB and J01FA01).

Narrow-spectrum phenoxymethylpenicillin is the antibiotic of choice for respiratory tract infections in Scandinavian countries, while broader-spectrum amoxicillin is used in most other countries of the European Region (Skarpeid & Høye, 2018). Similarly, not all AMC Network countries have marketing authorization for oral phenoxymethylpenicillin.

An alternative measure based on amoxicillin and phenoxymethylpenicillin consumption has been applied to global estimates of antibacterial consumption (Klein et al., 2020). The amoxicillin index (DIDs of amoxicillin and phenoxymethylpenicillin divided by the total DIDs) is applied in the analyses reported here. This metric compares the consumption of first-line and relatively narrower-spectrum penicillin antibiotics to that of broader-spectrum penicillins, cephalosporins and macrolides. Table 3.10 shows the volumes of consumption of amoxicillin and phenoxymethylpenicillin – in DID and percentage of total consumption of J01 antibacterials.

Table 3.8 Antibacterials at substance level (fifth ATC group level) that comprise DU75% (oral use), 2019

Agent (ATC)[a]	ARM	AZE	BIH	BLR	GEO	KGZ	MKD	MNE	RUS	SRB	SWI	TJK	TUR	UZB	Number of countries[b]	WHO/AMC[c]
Amoxicillin and beta-lactamase inhibitor (J01CR02)	3	3	1	2	1	8	1	2	2	2	1		1	7	13	1
Amoxicillin (J01CA04)	1	1	2	1	7	1		1	1	1	2	2		1	12	2
Doxycycline (J01AA02)	4	5		3	4	7		7	5	7	3		7		10	7
Sulfamethoxazole and trimethoprim (J01EE01)	6	6	6			6					7				5	
Nitrofurantoin (J01XE01)	7					4			9			5			4	10
Ampicillin (J01CA01)		8										3		6	3	
Cefalexin (J01DB01)			8					4		4					3	
Metronidazole (P01AB01)						9			8						2	
Tetracycline (J01AA07)		2													1	
Trimethoprim (J01EA01)					2										1	
Furazidin (J01XE03)				7											1	
Azithromycin (J01FA10)	2	7	4	4	3	3	6	3	3	3	8	4		3	13	4
Ciprofloxacin (J01MA02)	5		3		6	2	5	6	4	6	4	1	4	2	12	3
Clarithromycin (J01FA09)	8		7	5			2		7	5	5		2		8	5
Cefuroxime (J01DC02)			5	6			3				6		3	4	6	6
Cefixime (J01DD08)						5	4	5		8			5		5	9
Levofloxacin (J01MA12)		4			5	10			6					5	5	8
Cefaclor (J01DC04)													6		1	
Cefdinir (J01DD15)													8		1	

ATC: Anatomical Therapeutic Chemical (classification system); DU75%: antibacterial substances accounting for 75% of consumption.

[a] Agents included in this analysis: J01 antibacterials, neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), fidaxomicin (A07AA12), rifamycin oral (A07AA13), rifampicin (J04AB02), rifamycin intravenous (J04AB03), rifabutin (J04AB04), metronidazole (P01AB01), tinidazole (P01AB02), ornidazole (P01AB03) and secnidazole (P01AB07). [b] Numbers of countries that have this agent in DU75%. [c] WHO/AMC population-weighted mean for countries of the AMC Network.

Table 3.9 Antibacterials at substance level (fifth ATC group level) that comprise DU75% (parenteral use), 2019

Agent (ATC)[a]	ARM	AZE	BIH	BLR	GEO	KGZ	MNE	RUS	SRB	SWI	TJK	TUR	UZB	Number of countries[b]	WHO/AMC[c]
Metronidazole (J01XD01)	2	3	1	4	3	3	3	5	4		3			10	5
Cefazolin (J01DB04)			3	3		2		4	6	5	4	2	4	9	2
Gentamicin (J01GB03)			4				2		2		6	9		5	7
Ampicillin and beta-lactamase inhibitor (J01CR01)		4									5	5		3	
Amikacin (J01GB06)				6				3	5					3	8
Ampicillin (J01CA01)											2			1	
Benzylpenicillin (J01CE01)	4													1	
Benzathine benzylpenicillin (J01CE08)													6	1	
Flucloxacillin (J01CF05)										6				1	
Amoxicillin and beta-lactamase inhibitor (J01CR02)										1				1	
Clindamycin (J01FF01)												8		1	
Ceftriaxone (J01DD04)	1	2	2	1	1		1	1	1	2	1	1	1	12	1
Levofloxacin (J01MA12)				5	4			6	3				3	5	4
Cefotaxime (J01DD01)				2		1		2					7	4	3
Piperacillin and beta-lactamase inhibitor (J01CR05)										4		7		2	
Cefuroxime (J01DC02)										3		6		2	
Kanamycin (J01GB04)					2								5	2	9
Meropenem (J01DH02)												4		1	
Streptomycin (J01GA01)	3													1	
Ofloxacin (J01MA01)		1												1	
Moxifloxacin (J01MA14)												10		1	
Rifamycin (J04AB03)												3		1	
Combinations (J01CE30)[d]									7					1	
Combinations of penicillins (J01CR50)													2	1	6

ATC: Anatomical Therapeutic Chemical (classification system); DU75%: antibacterial substances accounting for 75% of consumption.

[a] Agents included in this analysis: J01 antibacterials, neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), fidaxomicin (A07AA12), rifamycin oral (A07AA13), rifampicin (J04AB02), rifamycin intravenous (J04AB03), rifabutin (J04AB04), metronidazole (P01AB01), tinidazole (P01AB02), ornidazole (P01AB03) and secnidazole (P01AB07). [b] Numbers of countries that have this agent in DU75%. [c] WHO/AMC population-weighted mean for countries of the AMC Network. [d] Combinations of benzylpenicillin and procaine penicillin.

Table 3.10 Consumption of oral amoxicillin and phenoxymethylpenicillin as a total of oral J01 consumption, 2019

Group of antibacterial agents	DDD/1000 inhabitants per day (% of total oral J01[a])													
	ARM	AZE	BIH	BLR	GEO	KGZ	MKD	MNE	RUS	SRB	SWI	TJK	TUR	UZB
Oral amoxicillin	1.5 (16%)	2.1 (22%)	2.7 (17%)	4.5 (22%)	0.8 (5%)	2.5 (22%)	1.3 (8%)	6.3 (25%)	2.4 (18%)	5.0 (20%)	1.1 (11%)	5.3 (31%)	1.0 (3%)	3.2 (20%)
Oral amoxicillin + phenoxymethyl-penicillin	1.5 (16%)	2.1 (22%)	3.3 (21%)	4.5 (22%)	0.8 (5%)	2.5 (22%)	1.3 (8%)	6.3 (25%)	2.4 (18%)	5.0 (20%)	1.2 (12%)	5.3 (31%)	1.1 (3%)	3.2 (20%)
Total oral J01	**9.7**	**9.5**	**16.1**	**20.5**	**14.7**	**11.3**	**15.6**	**24.7**	**13.3**	**24.7**	**9.8**	**17.4**	**31.5**	**15.5**

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

The amoxicillin index ranges from 5% in Georgia to 31% in Tajikistan. For almost all AMC Network countries there is little or no consumption of phenoxymethylpenicillin reported in 2019.

4. DISCUSSION

This report extends the analyses of data from the WHO Regional Office for Europe AMC Network – from the 2021 report of the WHO Regional Office for Europe and the 2019 and 2021 peer-reviewed articles by Robertson et al. (2019, 2021). The analyses focus on cross-national comparisons of consumption data for 2019 from 14 AMC Network countries.

In 2019, total consumption of antibacterials for systemic use (ATC J01) ranged from 10.6 DID for Switzerland to 33.2 DID for Türkiye. The median consumption was 19.6 DID. The arithmetic and population-weighted mean totals of J01 consumption in 2019 were 19.6 and 21.2 DID, respectively.

These consumption estimates were generally a little higher than those reported in 2018, where the range was 8.9 DID for Azerbaijan to 30.9 DID for Türkiye. The median consumption in 2018 was 18.8 DID, with arithmetic and population-weighted means of 17.5 and 18.5 DID, respectively. The reasons for these increases are not entirely clear. In formal analyses of trends over time, only two countries showed a statistically significant trend towards increased consumption of J01 antibacterials over the period 2014–2019 (Azerbaijan CAGR +13.8%, Russian Federation +3.2%). In the case of Azerbaijan, the increases are from a low baseline estimate of total consumption of J01 antibacterials in 2014 (6.4 DID). Previous AMC Network reports have suggested potential issues in the completeness of data capture and/or poor access to some antibiotics in Azerbaijan. The increased consumption recorded in 2019 (10.8 DID) suggests that some of these issues are being addressed.

As in previous analyses of AMC Network data, there were large variations in the extent of consumption of parenteral antibacterials, ranging from 5% of J01 consumption in Türkiye to 49% in Kyrgyzstan. Two other countries reported parenteral consumption of more than 20% of total J01 consumption in 2019 – Tajikistan (24%) and Uzbekistan (30%). The wide range of parenteral consumption is likely to reflect, in part, prescribing practices and cultural preferences. As oral administration generally is regarded as the most acceptable and economical method of administration of antimicrobials, high levels of consumption of parenteral formulations remain a potential target for interventions and behaviour change.

There was considerable variation in the extent of consumption of the pharmacological subgroups of J01. For example, in 2019, consumption of beta-lactam penicillins (J01C) ranged from 17% (Kyrgyzstan) to 43% (North Macedonia). Cephalosporin (J01D) consumption varied from 6% (Azerbaijan) to 38% (Kyrgyzstan), while quinolone (J01M) consumption varied from 7% (Montenegro) to 28% (Tajikistan). The reasons for these large variations across AMC Network countries require further investigation, including review of prescribing practices, clinical guidelines and treatment algorithms. High levels of consumption of quinolone antibacterials are of particular concern considering the 2019 European Medicines Agency recommendations for suspension of marketing authorization of medicines containing cinoxacin, flumequine, nalidixic acid and pipemidic acid, and restrictions on the circumstances in which quinolone medicines should be prescribed (European Medicines Agency, 2019).

In 2019, consumption of Access agents comprised between 35% (Uzbekistan) and 70% (Azerbaijan) of total antibacterial consumption. Data for Azerbaijan indicate increased total consumption of J01 antibacterials from 6.4 DID and 7.4 DID in 2014 and 2015, respectively, to 10.8 DID in 2019. Over the same time period, the proportion of consumption that was Access agents increased from 54%

in 2014 to 69% in 2019. This suggests that increased consumption can be directed towards Access antibiotics with lower resistance potential.

Watch group agents represented between 28% (Azerbaijan) and 58% (Uzbekistan) of total consumption. High levels of consumption of Watch group antibacterials suggest targets for further investigation, interventions and stewardship activities.

Consumption of Reserve agents remained low across all years of data analysed. The low levels reflect the analysis of data on total consumption combining community and hospital sectors; different consumption patterns would be expected in analyses of hospital data alone. Analyses based on the WHO AWaRe classification can support antimicrobial stewardship efforts and focus attention on prescribing practices that should be reviewed further. In 2019, five AMC Network countries met WHO's suggested national target of 60% of total consumption of antibacterials being derived from the Access list. Bosnia and Herzegovina was the only AMC Network country to achieve this target in each of the six years analysed (2014–2019).

Population-weighted estimates across the AMC Network in 2019 show that 50.6% of consumption was Access agents, 46.7% Watch agents, 0.2% Reserve agents and 2.5% unclassified agents. In 2018, the comparable estimates were 46.9%, 49.5%, 0.1% and 3.5%. These results suggest that along with increased total consumption across the network in 2019, there have been some positive changes with increased relative consumption of Access agents and decreased relative consumption of Watch agents.

The DU75% represents the antibacterial substances accounting for 75% of consumption measured in DDD and was calculated for oral and parenteral formulations separately. At country level, results are shown as the ranking of consumption at substance level, volumes of consumption in DID and assignment according to the AWaRe classification.

In 2019, the number of agents constituting the DU75% – by oral substance – ranged from 5 to 10 across the AMC Network countries. There were 10 agents in the population-weighted DU75% for the AMC Network – four Access and six Watch agents. The Watch agents ciprofloxacin and azithromycin were ranked three and four in relative consumption across the AMC Network. Relatively higher levels of consumption of specific Watch group antibiotics can suggest targets for further investigation, interventions and stewardship activities, including review of clinical guidelines and prescribing algorithms.

The analyses in this report focus on total consumption of antibacterials. Disaggregation of data to hospital and community sectors was not possible in most AMC Network countries, but this is an important area for future development as countries strengthen and enhance their surveillance capacity. Disaggregation of data to community and hospital sectors facilitates monitoring through using sector-specific metrics for quantifying antibiotic use and assessing the quality of prescribing.

The limitations of some of the data have implications for interpretation of results. Only medicines with an assigned ATC code and DDD are included in the analyses. Where there are medicines without codes consumed by the population, DID estimates will be underestimated. While import records have limitations, they will include the over-the-counter supply of antibacterials without prescription that occurs in some countries and areas. Aggregate data are used in the analyses presented here. Without information on indication for treatment, some results are difficult to interpret. A fuller interpretation of the consumption data requires an understanding of the local context.

Despite some data limitations, the levels of consumption reported and, in some cases, the choices of antimicrobial agents used, confirm the need for action. The cross-national comparisons in this report allow benchmarking of activities across the AMC Network. Direct comparisons between

estimates in 2019 and 2018 are hampered by differences in the countries included in the analyses – 17 countries in 2018 and 14 in 2019. However, substantial differences in the volumes and patterns of consumption between countries can suggest targets 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.

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ANNEX. AGENTS INCLUDED IN THE 2021 AWARE INDEX

Table A1.1. Access antibiotics 2021

Antibiotic	Class	ATC code	Listed on EML 2021
Amikacin	Aminoglycosides	J01GB06	Yes
Amoxicillin	Penicillins	J01CA04	Yes
Amoxicillin/clavulanic-acid	Beta-lactam/beta-lactamase-inhibitor	J01CR02	Yes
Ampicillin	Penicillins	J01CA01	Yes
Ampicillin/sulbactam	Beta-lactam/beta-lactamase-inhibitor	J01CR01	No
Azidocillin	Penicillins	J01CE04	No
Bacampicillin	Penicillins	J01CA06	No
Benzathine-benzylpenicillin	Penicillins	J01CE08	Yes
Benzylpenicillin	Penicillins	J01CE01	Yes
Brodimoprim	Trimethoprim-derivatives	J01EA02	No
Cefacetrile	First-generation-cephalosporins	J01DB10	No
Cefadroxil	First-generation-cephalosporins	J01DB05	No
Cefalexin	First-generation-cephalosporins	J01DB01	Yes
Cefaloridine	First-generation-cephalosporins	J01DB02	No
Cefalotin	First-generation-cephalosporins	J01DB03	No
Cefapirin	First-generation-cephalosporins	J01DB08	No
Cefatrizine	First-generation-cephalosporins	J01DB07	No
Cefazedone	First-generation-cephalosporins	J01DB06	No
Cefazolin	First-generation-cephalosporins	J01DB04	Yes
Cefradine	First-generation-cephalosporins	J01DB09	No
Cefroxadine	First-generation-cephalosporins	J01DB11	No
Ceftezole	First-generation-cephalosporins	J01DB12	No
Chloramphenicol	Amphenicols	J01BA01	Yes
Clindamycin	Lincosamides	J01FF01	Yes
Clometocillin	Penicillins	J01CE07	No
Cloxacillin	Penicillins	J01CF02	Yes
Dicloxacillin	Penicillins	J01CF01	No
Doxycycline	Tetracyclines	J01AA02	Yes
Epicillin	Penicillins	J01CA07	No
Flucloxacillin	Penicillins	J01CF05	No
Furazidin	Nitrofuran derivatives	J01XE03	No
Gentamicin	Aminoglycosides	J01GB03	Yes
Hetacillin	Penicillins	J01CA18	No
Mecillinam	Penicillins	J01CA11	No
Metampicillin	Penicillins	J01CA14	No
Meticillin	Penicillins	J01CF03	No
Metronidazole_IV	Imidazoles	J01XD01	Yes
Metronidazole_oral	Imidazoles	P01AB01	Yes

Antibiotic	Class	ATC code	Listed on EML 2021
Nafcillin	Penicillins	J01CF06	No
Nifurtoinol	Nitrofuran derivatives	J01XE02	No
Nitrofurantoin	Nitrofuran-derivatives	J01XE01	Yes
Ornidazole_IV	Imidazoles	J01XD03	No
Ornidazole_oral	Imidazoles	P01AB03	No
Oxacillin	Penicillins	J01CF04	No
Penamecillin	Penicillins	J01CE06	No
Phenoxymethylpenicillin	Penicillins	J01CE02	Yes
Pivampicillin	Penicillins	J01CA02	No
Pivmecillinam	Penicillins	J01CA08	No
Procaine-benzylpenicillin	Penicillins	J01CE09	Yes
Propicillin	Penicillins	J01CE03	No
Secnidazole	Imidazoles	P01AB07	No
Spectinomycin	Aminocyclitols	J01XX04	Yes
Sulbactam	Beta-lactamase-inhibitors	J01CG01	No
Sulfadiazine	Sulfonamides	J01EC02	No
Sulfadiazine/tetroxoprim	Sulfonamide-trimethoprim-combinations	J01EE06	No
Sulfadiazine/trimethoprim	Sulfonamide-trimethoprim-combinations	J01EE02	No
Sulfadimethoxine	Sulfonamides	J01ED01	No
Sulfadimidine	Sulfonamides	J01EB03	No
Sulfadimidine/trimethoprim	Sulfonamide-trimethoprim-combinations	J01EE05	No
Sulfafurazole	Sulfonamides	J01EB05	No
Sulfaisodimidine	Sulfonamides	J01EB01	No
Sulfalene	Sulfonamides	J01ED02	No
Sulfamazone	Sulfonamides	J01ED09	No
Sulfamerazine	Sulfonamides	J01ED07	No
Sulfamerazine/trimethoprim	Sulfonamide-trimethoprim-combinations	J01EE07	No
Sulfamethizole	Sulfonamides	J01EB02	No
Sulfamethoxazole	Sulfonamides	J01EC01	No
Sulfamethoxazole/trimethoprim	Sulfonamide-trimethoprim-combinations	J01EE01	Yes
Sulfamethoxypyridazine	Sulfonamides	J01ED05	No
Sulfametomidine	Sulfonamides	J01ED03	No
Sulfametoxydiazine	Sulfonamides	J01ED04	No
Sulfametrole/trimethoprim	Sulfonamide-trimethoprim-combinations	J01EE03	No
Sulfamoxole	Sulfonamides	J01EC03	No
Sulfamoxole/trimethoprim	Sulfonamide-trimethoprim-combinations	J01EE04	No
Sulfanilamide	Sulfonamides	J01EB06	No
Sulfaperin	Sulfonamides	J01ED06	No
Sulfaphenazole	Sulfonamides	J01ED08	No
Sulfapyridine	Sulfonamides	J01EB04	No
Sulfathiazole	Sulfonamides	J01EB07	No
Sulfathiourea	Sulfonamides	J01EB08	No
Sultamicillin	Beta-lactam/beta-lactamase-inhibitor	J01CR04	No
Talampicillin	Penicillins	J01CA15	No
Tetracycline	Tetracyclines	J01AA07	No
Thiamphenicol	Amphenicols	J01BA02	No
Tinidazole_IV	Imidazoles	J01XD02	No
Tinidazole_oral	Imidazoles	P01AB02	No
Trimethoprim	Trimethoprim-derivatives	J01EA01	Yes

ATC: Anatomical Therapeutic Chemical (classification system); EML: Essential Medicines List.

Table A1.2. Watch antibiotics 2021

Antibiotic	Class	ATC code	Listed on EML 2021
Arbekacin	Aminoglycosides	J01GB12	No
Aspoxicillin	Penicillins	J01CA19	No
Azithromycin	Macrolides	J01FA10	Yes
Azlocillin	Penicillins	J01CA09	No
Bekanamycin	Aminoglycosides	J01GB13	No
Biapenem	Carbapenems	J01DH05	No
Carbenicillin	Penicillins	J01CA03	No
Carindacillin	Penicillins	J01CA05	No
Cefaclor	Second-generation-cephalosporins	J01DC04	No
Cefamandole	Second-generation-cephalosporins	J01DC03	No
Cefbuperazone	Second-generation-cephalosporins	J01DC13	No
Cefcapene-pivoxil	Third-generation-cephalosporins	J01DD17	No
Cefdinir	Third-generation-cephalosporins	J01DD15	No
Cefditoren-pivoxil	Third-generation-cephalosporins	J01DD16	No
Cefepime	Fourth-generation-cephalosporins	J01DE01	No
Cefetamet-pivoxil	Third-generation-cephalosporins	J01DD10	No
Cefixime	Third-generation-cephalosporins	J01DD08	Yes
Cefmenoxime	Third-generation-cephalosporins	J01DD05	No
Cefmetazole	Second-generation-cephalosporins	J01DC09	No
Cefminox	Second-generation-cephalosporins	J01DC12	No
Cefodizime	Third-generation-cephalosporins	J01DD09	No
Cefonicid	Second-generation-cephalosporins	J01DC06	No
Cefoperazone	Third-generation-cephalosporins	J01DD12	No
Ceforanide	Second-generation-cephalosporins	J01DC11	No
Cefoselis	Fourth-generation-cephalosporins	to be assigned	No
Cefotaxime	Third-generation-cephalosporins	J01DD01	Yes
Cefotetan	Second-generation-cephalosporins	J01DC05	No
Cefotiam	Second-generation-cephalosporins	J01DC07	No
Cefoxitin	Second-generation-cephalosporins	J01DC01	No
Cefozopran	Fourth-generation-cephalosporins	J01DE03	No
Cefpiramide	Third-generation-cephalosporins	J01DD11	No
Cefpirome	Fourth-generation-cephalosporins	J01DE02	No
Cefpodoxime-proxetil	Third-generation-cephalosporins	J01DD13	No
Cefprozil	Second-generation-cephalosporins	J01DC10	No
Cefsulodin	Third-generation-cephalosporins	J01DD03	No
Ceftazidime	Third-generation-cephalosporins	J01DD02	Yes
Cefteram-pivoxil	Third-generation-cephalosporins	J01DD18	No
Ceftibuten	Third-generation-cephalosporins	J01DD14	No
Ceftizoxime	Third-generation-cephalosporins	J01DD07	No
Ceftriaxone	Third-generation-cephalosporins	J01DD04	Yes
Cefuroxime	Second-generation-cephalosporins	J01DC02	Yes
Chlortetracycline	Tetracyclines	J01AA03	No
Cinoxacin	Quinolones	J01MB06	No
Ciprofloxacin	Fluoroquinolones	J01MA02	Yes
Clarithromycin	Macrolides	J01FA09	Yes
Clofoctol	Phenol derivatives	J01XX03	No
Clomocycline	Tetracyclines	J01AA11	No
Delafloxacin	Fluoroquinolones	J01MA23	No

Antibiotic	Class	ATC code	Listed on EML 2021
Demeclocycline	Tetracyclines	J01AA01	No
Dibekacin	Aminoglycosides	J01GB09	No
Dirithromycin	Macrolides	J01FA13	No
Doripenem	Carbapenems	J01DH04	No
Enoxacin	Fluoroquinolones	J01MA04	No
Ertapenem	Carbapenems	J01DH03	No
Erythromycin	Macrolides	J01FA01	No
Fidaxomicin	Macrolides	A07AA12	No
Fleroxacin	Fluoroquinolones	J01MA08	No
Flomoxef	Second-generation-cephalosporins	J01DC14	No
Flumequine	Quinolones	J01MB07	No
Flurithromycin	Macrolides	J01FA14	No
Fosfomycin_oral	Phosphonics	J01XX01	No
Fusidic-acid	Steroid antibacterials	J01XC01	No
Garenoxacin	Fluoroquinolones	J01MA19	No
Gatifloxacin	Fluoroquinolones	J01MA16	No
Gemifloxacin	Fluoroquinolones	J01MA15	No
Grepafloxacin	Fluoroquinolones	J01MA11	No
Imipenem/cilastatin	Carbapenems	J01DH51	No
Isepamicin	Aminoglycosides	J01GB11	No
Josamycin	Macrolides	J01FA07	No
Kanamycin_IV	Aminoglycosides	J01GB04	No
Kanamycin_oral	Aminoglycosides	A07AA08	No
Lascufloxacin	Fluoroquinolones	J01MA25	No
Latamoxef	Third-generation-cephalosporins	J01DD06	No
Levofloxacin	Fluoroquinolones	J01MA12	No
Levonadifloxacin	Fluoroquinolones	J01MA24	No
Lincomycin	Lincosamides	J01FF02	No
Lomefloxacin	Fluoroquinolones	J01MA07	No
Loracarbef	Second-generation-cephalosporins	J01DC08	No
Lymecycline	Tetracyclines	J01AA04	No
Meropenem	Carbapenems	J01DH02	Yes
Metacycline	Tetracyclines	J01AA05	No
Mezlocillin	Penicillins	J01CA10	No
Micronomicin	Aminoglycosides	to be assigned	No
Midecamycin	Macrolides	J01FA03	No
Minocycline_oral	Tetracyclines	J01AA08	No
Miocamycin	Macrolides	J01FA11	No
Moxifloxacin	Fluoroquinolones	J01MA14	No
Nemonoxacin	Quinolones	J01MB08	No
Neomycin_IV	Aminoglycosides	J01GB05	No
Neomycin_oral	Aminoglycosides	A07AA01	No
Netilmicin	Aminoglycosides	J01GB07	No
Norfloxacin	Fluoroquinolones	J01MA06	No
Ofloxacin	Fluoroquinolones	J01MA01	No
Oleandomycin	Macrolides	J01FA05	No
Oxolinic-acid	Quinolones	J01MB05	No
Oxytetracycline	Tetracyclines	J01AA06	No
Panipenem	Carbapenems	J01DH55	No
Pazufloxacin	Fluoroquinolones	J01MA18	No

Antibiotic	Class	ATC code	Listed on EML 2021
Pefloxacin	Fluoroquinolones	J01MA03	No
Penimepicycline	Tetracyclines	J01AA10	No
Pheneticillin	Penicillins	J01CE05	No
Pipemidic-acid	Quinolones	J01MB04	No
Piperacillin	Penicillins	J01CA12	No
Piperacillin/tazobactam	Beta-lactam/beta-lactamase-inhibitor_anti-pseudomonal	J01CR05	Yes
Piromidic-acid	Quinolones	J01MB03	No
Pristinamycin	Streptogramins	J01FG01	No
Prulifloxacin	Fluoroquinolones	J01MA17	No
Ribostamycin	Aminoglycosides	J01GB10	No
Rifabutin	Rifamycins	J04AB04	No
Rifampicin	Rifamycins	J04AB02	No
Rifamycin_IV	Rifamycins	J04AB03	No
Rifamycin_oral	Rifamycins	A07AA13	No
Rifaximin	Rifamycins	A07AA11	No
Rokitamycin	Macrolides	J01FA12	No
Rolitetracycline	Tetracyclines	J01AA09	No
Rosoxacin	Quinolones	J01MB01	No
Roxithromycin	Macrolides	J01FA06	No
Rufloxacin	Fluoroquinolones	J01MA10	No
Sarecycline	Tetracyclines	J01AA14	No
Sisomicin	Aminoglycosides	J01GB08	No
Sitafloxacin	Fluoroquinolones	J01MA21	No
Solithromycin	Macrolides	J01FA16	No
Sparfloxacin	Fluoroquinolones	J01MA09	No
Spiramycin	Macrolides	J01FA02	No
Spiramycin/metronidazole	Antibacterials_combinations	J01RA04	No
Streptoduocin	Aminoglycosides	J01GA02	No
Streptomycin_IV	Aminoglycosides	J01GA01	No
Streptomycin_oral	Aminoglycosides	A07AA04	No
Sulbenicillin	Penicillins	J01CA16	No
Tazobactam	Beta-lactamase-inhibitors	J01CG02	No
Tebipenem	Carbapenems	J01DH06	No
Teicoplanin	Glycopeptides	J01XA02	No
Telithromycin	Macrolides	J01FA15	No
Temafloxacin	Fluoroquinolones	J01MA05	No
Temocillin	Penicillins	J01CA17	No
Ticarcillin	Penicillins	J01CA13	No
Tobramycin	Aminoglycosides	J01GB01	No
Tosufloxacin	Fluoroquinolones	J01MA22	No
Troleandomycin	Macrolides	J01FA08	No
Trovafloxacin	Fluoroquinolones	J01MA13	No
Vancomycin_IV	Glycopeptides	J01XA01	Yes
Vancomycin_oral	Glycopeptides	A07AA09	Yes

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Table A1.3. Reserve antibiotics 2021

Antibiotic	Class	ATC code	Listed on EML 2021
Aztreonam	Monobactams	J01DF01	No
Carumonam	Monobactams	J01DF02	No
Cefiderocol[a]	Other-cephalosporins	J01DI04	Yes
Ceftaroline-fosamil	Fifth-generation cephalosporins	J01DI02	No
Ceftazidime/avibactam	Third-generation-cephalosporins	J01DD52	Yes
Ceftobiprole-medocaril	Fifth-generation cephalosporins	J01DI01	No
Ceftolozane/tazobactam	Fifth-generation cephalosporins	J01DI54	No
Colistin_IV	Polymyxins	J01XB01	Yes
Colistin_oral	Polymyxins	A07AA10	No
Dalbavancin	Glycopeptides	J01XA04	No
Dalfopristin/quinupristin	Streptogramins	J01FG02	No
Daptomycin	Lipopeptides	J01XX09	No
Eravacycline	Tetracyclines	J01AA13	No
Faropenem	Penems	J01DI03	No
Fosfomycin_IV	Phosphonics	J01XX01	Yes
Iclaprim	Trimethoprim-derivatives	J01EA03	No
Imipenem/cilastatin/relebactam	Carbapenems	J01DH56	No
Lefamulin	Pleuromutilin	J01XX12	No
Linezolid	Oxazolidinones	J01XX08	Yes
Meropenem/vaborbactam	Carbapenems	J01DH52	Yes
Minocycline_IV	Tetracyclines	J01AA08	No
Omadacycline	Tetracyclines	J01AA15	No
Oritavancin	Glycopeptides	J01XA05	No
Plazomicin	Aminoglycosides	J01GB14	Yes
Polymyxin-B_IV	Polymyxins	J01XB02	Yes
Polymyxin-B_oral	Polymyxins	A07AA05	No
Tedizolid	Oxazolidinones	J01XX11	No
Telavancin	Glycopeptides	J01XA03	No
Tigecycline	Glycylcyclines	J01AA12	No

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[a] New addition to EML 2021.

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World Health Organization
Regional Office for Europe
UN City, Marmorvej 51,
DK-2100 Copenhagen Ø, Denmark
Tel.: +45 45 33 70 00 Fax: +45 45 33 70 01
Email: eurocontact@who.int
Website: www.who.int/europe