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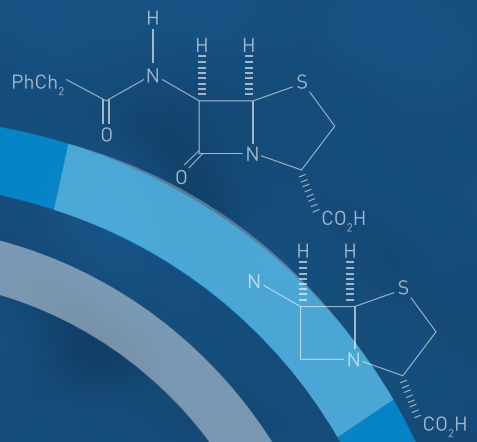

WHO Regional Office for Europe Antimicrobial Medicines Consumption (AMC) Network

AMC data 2020–2021

Abstract

This report presents analyses of data on antimicrobial medicines consumption collected from non-European Union countries in the WHO European Region – 13 countries provided 2020 data and 10 countries provided 2021 data. The analyses show the results for key metrics of antibiotic consumption including total use, relative use of agents according to the WHO Access, Watch and Reserve (AWaRe) classification, and concordance with WHO monitoring indicators for responsible use of antibiotics. Analyses explore the possible impact of the COVID-19 epidemic on volumes and patterns of consumption of antibiotics.

Keywords

CONSUMPTION
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RESPONSIBLE USE OF ANTIBACTERIALS
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ABBREVIATIONS

AMC	Antimicrobial Medicines Consumption (Network)
AMR	antimicrobial resistance
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
EEA	European Economic Area
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
GLASS	Global Antimicrobial Resistance and Use Surveillance System
GLASS-AMC	Global Antimicrobial Resistance and Use Surveillance System, Antimicrobial Medicines Consumption module
GLASS-IT	Global Antimicrobial Resistance and Use Surveillance System Information Technology

Abbreviations of country names used in 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 Regional Office for Europe Antimicrobial Medicines Consumption (AMC) Network aims to support all Member States 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). AMC Network members are: 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.

This is the fifth AMC Network report, with analyses conducted using 2020 data from 13 AMC Network countries and 2021 data from 10 countries. The report focuses on cross-national analyses and trends from 2019 to 2021, which might reflect the impact of the early phases of the COVID-19 pandemic. The 2021 WHO Access, Watch and Reserve (AWaRe) classification of antibiotics is applied and the WHO national monitoring target of at least 60% of total consumption being Access agents is assessed. The utilization of antibacterial substances accounting for 75% of consumption (the drug utilization 75% (DU75%)) measured in defined daily doses, is calculated for oral and parenteral formulations separately. The impact of using different population estimates in the Global Antimicrobial Resistance and Use Surveillance System (GLASS) is explored.

Key findings

Data on total consumption of antibacterials for systemic use (Anatomical Therapeutic Chemical (ATC) classification group J01) were available for 13 countries in 2020 and 10 in 2021. In 2020, consumption of J01 antibacterials ranged from 9.0 defined daily doses per 1000 inhabitants per day (DID) (Switzerland) to 34.3 DID (Kyrgyzstan), with a median consumption of 19.5 DID and a population-weighted mean consumption of 21.8 DID. The comparable estimates for 2019 were 10.6–33.2 DID, a median consumption of 19.6 DID and a population-weighted mean consumption 21.2 DID. Of 10 countries with 2021 data, consumption ranged from 8.6 DID (Switzerland) to 34.4 DID (Serbia), with a median consumption of 19.3 DID and a population-weighted mean consumption of 20.3 DID.

Together, the three years of data (2019–2021) suggest there was increased consumption of J01 antibacterials in 2020 and the early phases of the COVID-19 pandemic, and subsequent reductions in 2021. However, this pattern was not consistent across all countries. Data from Belarus, the Russian Federation and Tajikistan followed the pattern, showing increases in consumption from 2019 to 2020, then falling consumption levels in 2021. Consumption in Serbia increased in each successive year from 26.6 DID in 2019, to 29.2 DID in 2020 and to 34.4 DID in 2021. In Türkiye, total consumption fell substantially between 2019 and 2020 (33.2 DID to 25.8 DID) before increasing in 2021 to 28.3 DID. Further investigation at the country level is needed to understand the reasons for the patterns seen and the possible contribution of the COVID-19 pandemic to the estimates.

AMC population-weighted estimates for consumption of pharmacological subgroups of J01 antibacterials in 2019, 2020 and 2021 showed increased relative consumption of the macrolides, lincosamides and streptogramins group (J01F), increasing from 14% of total J01 consumption in 2019 to 20% in 2020, then falling to 15% in 2021. The macrolides group includes azithromycin, which was promoted as a treatment for COVID-19 infection. Subsequent clinical trials failed to demonstrate any clinical benefits of azithromycin in reducing the time to recovery or the risk of hospitalization for people

with suspected COVID-19 in the community. This trial evidence may have contributed to the reduced consumption of J01F antibacterials and, in particular, azithromycin in 2021.

Ten countries had consumption estimates available for all years 2014–2021. Three showed statistically significant increases in consumption of J01 antibacterials over the eight years of data collection – Azerbaijan (compound annual growth rate (CAGR) +8.4%), Bosnia and Herzegovina (+3.1%) and the Russian Federation (+2.8%). Three countries showed statistically significant reductions in consumption over time – North Macedonia (–0.9%), Switzerland (–3.6%) and Türkiye (–2.9%).

AMC Network population-weighted estimates of the relative consumption of Access, Watch and Reserve classification antibacterials from 2019 to 2021 show that Access agents represented 50% of consumption in 2019, 47% in 2020 and 50% in 2021. Watch group antibiotics constituted 46%, 52% and 49% of total consumption in the same years. Consumption of Reserve agents and unclassified antibacterials was low in all three years. Most countries showed patterns similar to the Network averages, namely decreases in relative consumption of Access agents from 2019 to 2020 and increases in 2021. This pattern of consumption is likely to be attributable to the increased consumption of Watch group macrolides, including azithromycin, in 2020 and reductions in 2021.

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. Only Switzerland achieved this target in 2020 (63%); Belarus (66%) and Switzerland (65%) met it in 2021.

The number of agents constituting the DU75% – by oral substance – ranged from 5 to 10 in 2020 and 6 to 9 in 2021 across the AMC Network countries. There were six Watch agents in the population-weighted DU75% in both 2020 and 2021. The most notable change between 2019 and 2020 was the increased relative consumption of azithromycin – rising from fourth to second-most consumed oral antibiotic across the AMC Network in 2020. The pattern was consistent, with azithromycin included in the DU75% for 12 of the 13 Network countries for which data was available in 2020, ranked first most consumed antibiotic in six countries and second in a further five countries.

The scope of WHO's GLASS has widened in the past few years to include surveillance data on AMC. This module is called GLASS-AMC and the platform is called GLASS information technology (GLASS-IT) platform. Network members are transitioning to data collection via the GLASS-IT platform. Analyses are broadly similar to those conducted by the AMC Network, except that GLASS-AMC applies United Nations population estimates for its calculations. Since 2011, the AMC Network has used World Bank population estimates in calculations – apart from for Switzerland and Türkiye, where national population estimates are applied. Exploratory analyses were conducted using 2021 consumption data to examine the impact of a change in population data source (from World Bank to United Nations population estimates). In six of seven countries which have been using World Bank population estimates in calculations of antimicrobial consumption, these population estimates were lower than United Nations estimates, with the largest differences for Belarus (2.85% lower) and Serbia (7.13% lower). For Serbia, the total consumption estimate is 6.7% higher using the World Bank population estimate rather than that of the United Nations. For Switzerland and Türkiye, national population estimates are higher than United Nations estimates, 4.48% higher in the case of Türkiye. For Türkiye, this results in an estimate of total consumption of J01 antibacterials that is 4.69% lower than that derived using United Nations population data.

These findings are relevant as countries move to AMC consumption calculated using the GLASS-IT platform. Those interpreting and using consumption estimates to inform national policies on access and use of antibiotics need to be aware of the data source used in the calculations, particularly in the situation that historical data based on World Bank population estimates are being compared with new GLASS-AMC estimates. The GLASS-IT platform will recalculate historical data and adjust populations used in the calculations to United Nations estimates, however this can only occur for historical data that are uploaded to the GLASS-IT platform.

1. INTRODUCTION

1.1 Background

Antimicrobial resistance (AMR) is a serious threat to public health. A comprehensive analysis of regional and country-level estimates of AMR burden in the WHO European Region estimated 541 000 deaths (95% uncertainty interval 370 000–763 000) associated with bacterial AMR,1 and 133 000 deaths (90 100–188 000) attributable to bacterial AMR in 20192 (European Antimicrobial Resistance Collaborators, 2022). Ensuring prudent antimicrobial use is a key priority in an effective response to the challenges of AMR. Regular surveillance of antibiotic consumption to identify potential overuse, underuse and inappropriate use can help identify potential targets for interventions to improve antibiotic utilization.

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

The WHO Regional Office for Europe AMC Network has been undertaking systematic surveillance of antimicrobial medicines consumption in 18 non-European Union (EU) Member States of the WHO European Region since 2011 (WHO Regional Office for Europe, 2022a). 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, 2022).

The following Member States 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.

1.3 Previous publications of AMC Network data

There have been four published reports of AMC Network data. The first report covered data for 2011–2014, and was published in 2017 (WHO Regional Office for Europe, 2017). An analysis of data for 2011–2017 for 17 Network members was 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); and 2019 data for 14 AMC Network countries was published in 2022 (WHO Regional Office for Europe, 2022a).

Analyses of AMC Network data have also been published in the peer-reviewed literature: a cross-national comparison of 2015 AMC data for 16 members of the AMC Network was published in 2019 (Robertson et al., 2019) and 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 was published in 2021 (Robertson et al., 2021).

1 Based on an alternative scenario in which all drug-resistant infections were replaced by drug-susceptible infections.
2 Based on an alternative scenario in which all drug-resistant infections were replaced by no infection.

1.4 Scope and aim of this report

This report extends the reporting of the AMC Network, presenting data for 2020 (13 countries) and 2021 (10 countries) from members that submitted data and gave permission for it to be published. Cross-national comparisons are presented. Comparisons with 2019 consumption data are also made to examine the possible impacts of the COVID-19 pandemic on the volumes and patterns of consumption of antibacterial agents.

The analyses apply the 2021 Access, Watch and Reserve (AWaRe) classification of antibiotics (WHO, 2021a, 2021b), 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). Finally, exploratory analyses are conducted to examine the potential impact of a change of source of population data on consumption estimates derived using the Global Antimicrobial Resistance and Use Surveillance System (GLASS) platform.

2. METHODS

2.1 Data sources and data collection

2.1.1 Data sources

AMC Network countries mostly rely on import data – using customs records and declaration forms, supplemented with sales records from market authorization holders, local manufacturing estimates, wholesaler records, commercial data and, in some cases, reimbursement data sources – to derive estimates of consumption (Table 1). In some countries, data are not available for all years examined.

Table 1 Sources of data used for consumption estimates, 2014–2021

Country	2014	2015	2016	2017	2018	2019	2020	2021
Albania	I	I	I	I	I	I	–	–
Armenia	I, M	I, M	I, M	I, M	I, M	I, M	I, M	–
Azerbaijan	I	I	I	I	I	I	I	I
Belarus	I, M	I, M	I, M	I, M	I, M	I, M	I, M[d]	I, M
Bosnia and Herzegovina	S, M	S, M	S, M	S, M	S, M	S, M	S, M	S, M
Georgia	I	I	I	I	I	I	I	–
Kazakhstan	–	S	S	S	S	–	–	–
Kyrgyzstan	–	I, S	I, S	I, S	I, S	I, S	I, S	–
Montenegro	S	S	S	S	S	S	S	S
North Macedonia[a]	R	R	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	S	S
Serbia	S	S	S	S	S	S	S	S
Switzerland[b]	S	S	S	S	S	S	S	S
Tajikistan	I, C	I, C	I, C	I, C	I, C	I, C	I, C	I, C
Türkiye[c]	S	S	S	S	S	S	S	S
Ukraine	S	S	S	S	S	–	–	–
Uzbekistan	–	–	I, S	I, S	I, S	I, S	–	–

Notes: 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 Sell-In data (sales data from wholesalers to pharmacy), self-dispending doctors and hospital, therefore covering outpatient and inpatient consumption.[3] [c] Türkiye uses wholesalers' records from the pharmaceutical track and trace system. [d] During the pandemic alternative suppliers were used to procure some medicines. Data from these suppliers were not included in these analyses. Therefore, estimates of total consumption and consumption of specific agents used to manage COVID-19 including azithromycin, clarithromycin and oseltamivir will be underestimates of actual consumption.
Source: AMC Network.

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.

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, 2017) and the *GLASS methodology for surveillance of national antimicrobial consumption* (WHO, 2020). 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.

2.2 ATC and DDD classification systems

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, 2022).

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.

Only medicines with an assigned ATC code and DDD are included in the analyses reported here. In several countries in the AMC Network, various 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 DDD per 1000 inhabitants per day (DID)estimates will underestimate total antimicrobial consumption in the country.

2.2.1 Population estimates

Population-adjusted estimates of consumption are derived by dividing the total number of DDDs at the desired ATC code level by the relevant population. For total consumption, this is the national population, which is assumed to reflect the potential scope of usage of the product.

Since 2011, the AMC Network has applied population estimates from the World Bank for the calculations, except for North Macedonia where the population eligible to receive medicines under the health insurance fund is used, and Switzerland and Türkiye, where national population estimates are applied. In the case of Switzerland, national estimates are used for the sake of consistency with the estimates published in their national reports; in the case of Türkiye, national estimates account for the large refugee populations in that country that are not reflected in World Bank population estimates.

For global reporting using the GLASS information technology (GLASS-IT) platform, WHO uses United Nations population statistics as standardized population estimates for all Member States. The GLASS methodology notes that for national reporting, countries should use the best estimates of the population covered by the surveillance system.

The impact of changing from World Bank to United Nations population statistics for deriving consumption estimates is explored in section 3.4.1 of this report.

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 outside the ATC J01 group are also included in the calculation of antimicrobial consumption according the 2021 WHO AWaRe classification (WHO, 2021b); these comprise: 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).

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, 2021a).

Table 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)

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, DID is calculated for the total population, including all age and gender groups.

Patterns of consumption in 2020 and 2021 by ATC 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 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).

2.4.1.2 Route of administration

Oral administration is generally regarded as the most acceptable and economical method of administration of antimicrobials. 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 the 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 the use of oral formulations without any loss of clinical efficacy.

2.4.1.3 Consumption of pharmacological subgroups (ATC 3rd level)

Absolute and relative consumption figures for pharmacological subgroups of J01 (ATC 3rd 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 and evaluated using analysis of variance (ANOVA) tests. P values ≤ 0.05 were considered statistically significant.

2.4.3 WHO AWaRe classification

The AWaRe classification of antibiotics was developed in 2017 by the WHO Expert Committee on Selection and Use of Essential Medicines as a tool to support antibiotic stewardship efforts at local, national and global levels. Antibiotics are classified into three groups, Access, Watch and Reserve, taking into account the impact of different antibiotics and antibiotic classes on AMR, to emphasize the importance of their appropriate use. The characteristics of these groups are shown in Table 3.

Subsequent updates to the AWaRe classification in 2019 (WHO, 2019) and 2021 (WHO, 2021b) have resulted in the classification of a total of 258 antibiotics.

The AWaRe classification is a useful tool for monitoring antibiotic consumption, defining targets and monitoring the effects of stewardship policies that aim to optimize antibiotic use and curb AMR. The WHO Thirteenth General Programme of Work 2019–2023 includes a country-level target of at least 60% of total antibiotic consumption being Access group antibiotics (WHO, 2018, 2021b).

The proportions of consumption (%) according to the AWaRe classification are presented in this report.

The agents listed in the 2021 AWaRe index are shown in Annex 1.

Table 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.

2.4.4 WHO global monitoring indicator

WHO has proposed a global monitoring indicator that by 2023, 60% of all antibiotics consumed should come from the Access group, those at lowest risk of resistance (WHO, 2021b).

The proportion of total consumption that comprised Access agents was calculated for each year of analysis from 2014 to 2021. The number of countries reaching the WHO global monitoring target in 2019 and across each of the years assessed is reported.

2.4.5 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 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 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 (ATC 5th group level). 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.

2.4.6 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 the DID 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, 2021).

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

2.4.7 Metrics reported in the analyses

The key metrics used in analyses and included in this report are summarized in Table 4.

Table 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	%
Concordance with WHO global monitoring indicator	
Proportion of total consumption that is Access agents	%
DU75%	
DU75% – oral formulation	Rank
DU75% – parenteral formulation	Rank
Summary metrics reported in cross-national comparisons	
Arithmetic mean estimates of: - total consumption of J01 antibacterials - consumption of pharmacological subgroups (ATC3) - 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) - consumption of agents according to AWaRe classification - agents comprising the DU75%	 DID DID, % DID, % Rank

[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 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. ANTIMICROBIAL MEDICINES CONSUMPTION ACROSS THE AMC NETWORK, 2020–2021

In this chapter, comparisons are made across AMC Network members providing consumption data for 2020 (13 countries) and 2021 (10 countries). Where possible, comparisons with 2019 (14 countries) are provided.

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

3.1.1 Total consumption in 2020

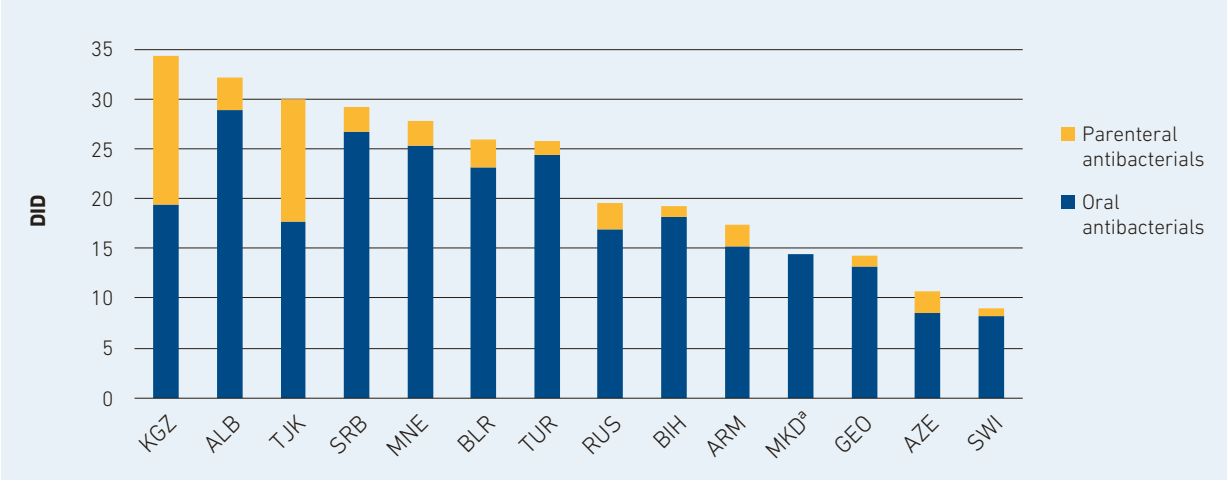
Consistent with previous analyses of AMC Network data, there is wide variability in reported total consumption of J01 antibacterials for systemic use (ATC class J01) for 2020 – ranging from 34.3 DID (Kyrgyzstan) to 9.0 DID (Switzerland) (Fig. 1 and Table 5). This compares to a range of 33.2 DID (Türkiye) to 10.6 DID (Switzerland) in 2019.

The median consumption in 2020 was 19.5 DID (in 2019 it was 19.6 DID across 14 network members). The arithmetic and population-weighted mean totals of J01 consumption in 2020 were 21.4 and 21.8 DID, respectively (compared to 19.6 and 21.2 DID in 2019).

3.1.2 Route of administration in 2020

The extent of consumption of parenteral formulations varied widely, from 6% in Bosnia and Herzegovina and Türkiye, up to 43% in Kyrgyzstan (Table 5). North Macedonia data relate to community consumption of oral antibiotics only.

Fig. 1 Total consumption of J01 antibacterials by route of administration in 2020



[a] Community consumption.

Table 5 Total consumption of J01 antibacterials by route of administration, 2020

Route of administration	DID (% of total[a])													
	KGZ	TJK	SRB	MNE	BLR	TUR	RUS	BIH	ARM	MKD[b]	GEO	AZE	SWI	WHO/AMC[c]
Oral J01	19.5 (57)	17.8 (59)	26.7 (91)	25.4 (91)	23.2 (89)	24.3 (94)	17 (87)	18.1 (94)	15.2 (88)	14.5 (100)	13.1 (92)	8.5 (79)	8.1 (91)	19.1 (88)
Parenteral J01	14.8 (43)	12.2 (41)	2.5 (9)	2.4 (9)	2.8 (11)	1.5 (6)	2.5 (13)	1.2 (6)	2.2 (12)	–	1.2 (8)	2.2 (21)	0.8 (9)	2.7 (12)
Total[a]	**34.3**	**30.0**	**29.2**	**27.8**	**25.9**	**25.8**	**19.5**	**19.2**	**17.4**	**14.5**	**14.3**	**10.8**	**9.0**	**21.8**

[a] Total amounts and percentages may vary slightly due to rounding. [b] Community consumption. [c] WHO/AMC population-weighted mean for countries of the AMC Network.

3.1.3 Total consumption in 2021

Total consumption of antibacterials for systemic use (ATC class J01) in 2021 is examined by route of administration (oral and parenteral formulations) (Fig. 2 and Table 6).

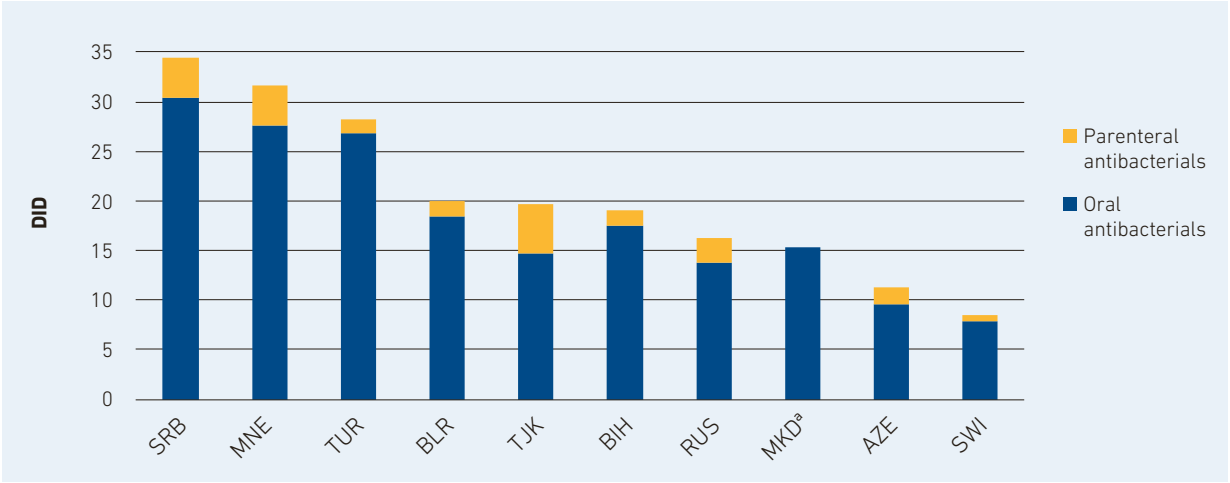
Consumption of J01 antibacterials in 2021 across the 10 countries ranged from 34.4 DID (Serbia) to 8.6 DID (Switzerland).

The median consumption in 2021 was 19.3 DID (in 2020 it was 22.7 DID across 13 network members). The arithmetic and population-weighted mean totals of J01 consumption in 2021 were 20.4 and 20.3 DID, respectively (compared to 22.1 and 21.9 DID in 2020).

3.1.4 Route of administration in 2021

The extent of consumption of parenteral formulations in 2021 varied from 5% in Türkiye up to 25% in Tajikistan (Table 6).

Fig. 2 Total consumption of J01 antibacterials by route of administration in 2021



[a] Community consumption

Table 6 Total consumption of J01 antibacterials by route of administration, 2021

Route of administration	DID (% of total[a])										
	SRB	MNE	TUR	BLR	TJK	BIH	RUS	MKD[b]	AZE	SWI	WHO/AMC[c]
Oral J01	30.4 (89)	27.6 (87)	26.8 (95)	18.5 (93)	14.7 (75)	17.5 (92)	13.8 (85)	15.3 (100)	9.5 (85)	7.8 (91)	18.2 (90)
Parenteral J01	3.9 (11)	4.1 (13)	1.4 (5)	1.5 (7)	4.9 (25)	1.5 (8)	2.4 (15)	–	1.7 (15)	0.8 (9)	2.1 (10)
Total[a]	**34.4**	**31.7**	**28.3**	**19.9**	**19.6**	**19.0**	**16.3**	**15.3**	**11.3**	**8.6**	**20.3**

[a] Total amounts and percentages may vary slightly due to rounding. [b] Community consumption [c] WHO/AMC population-weighted mean for countries of the AMC Network.

3.1.5 Changes in total consumption of J01 antibacterials 2019–2021

Table 7 shows summary total consumption metrics for AMC Network countries in 2019, 2020 and 2021.

Arithmetic mean and the WHO/AMC population-weighted consumption estimates were highest in 2020, reverting closer to 2019 levels in 2021. This is consistent with the pattern of increased consumption of antibacterial agents during 2020 and the early phases of the COVID-19 pandemic, and subsequent reductions as effective treatment regimens were identified, and agents promoted as potentially useful were shown to offer no benefits. Median consumption estimates were more stable over time, explained in part by variability in country-level consumption (Table 7).

Table 7 Metrics of total consumption of J01 antibacterials for AMC Network countries, 2019–2021

Year (Number of countries)	DID		
	Median consumption	Arithmetic mean consumption	Population-weighted consumption
2019 (n=14)	19.6	19.6	21.2
2020 (n=13)	19.5	21.4	21.8
2021 (n=10)	19.3	20.4	20.3

Consumption increased from 21.9 DID in 2019 to 34.3 DID in 2020 in Kyrgyzstan, and from 11.2 to 17.4 DID in Armenia, however no 2021 estimates were available for these two countries. Data from Belarus, the Russian Federation and Tajikistan showed increases in consumption from 2019 to 2020, then falling in 2021.

Consumption in Serbia, however, increased in each of the years – from 26.6 DID in 2019, to 29.2 DID in 2020 and 34.4 DID in 2021. In Montenegro, total consumption was similar in 2019 and 2020 at 27.1 DID and 27.8 DID respectively, increasing to 31.7 DID in 2021.

In Türkiye, total consumption fell substantially between 2019 and 2020 (33.2 DID to 25.8 DID) before increasing in 2021 to 28.3 DID (Table 8).

Further investigation at the country level is needed to understand the reasons for the patterns seen and the possible contribution of the COVID-19 pandemic to the estimates.

Table 8 Total consumption of J01 antibacterials 2019–2021

Year	DID														
	KGZ	TJK	SRB	MNE	BLR	TUR	RUS	BIH	ARM	MKD[a]	GEO	AZE	SWI	UZB	WHO/AMC[b]
2019	21.9	22.8	26.6	27.1	22.6	33.2	15.2	17.4	11.2	15.6	16.5	10.8	10.6	22.2	21.2
2020	34.3	30.0	29.2	27.8	25.9	25.8	19.5	19.2	17.4	14.5	14.3	10.8	9.0	–	21.8
2021	–	19.6	34.4	31.7	19.9	28.3	16.3	19.0	–	15.3	–	11.3	8.6	–	20.3

[a] Community consumption. [b] WHO/AMC population-weighted mean for countries of the AMC Network.

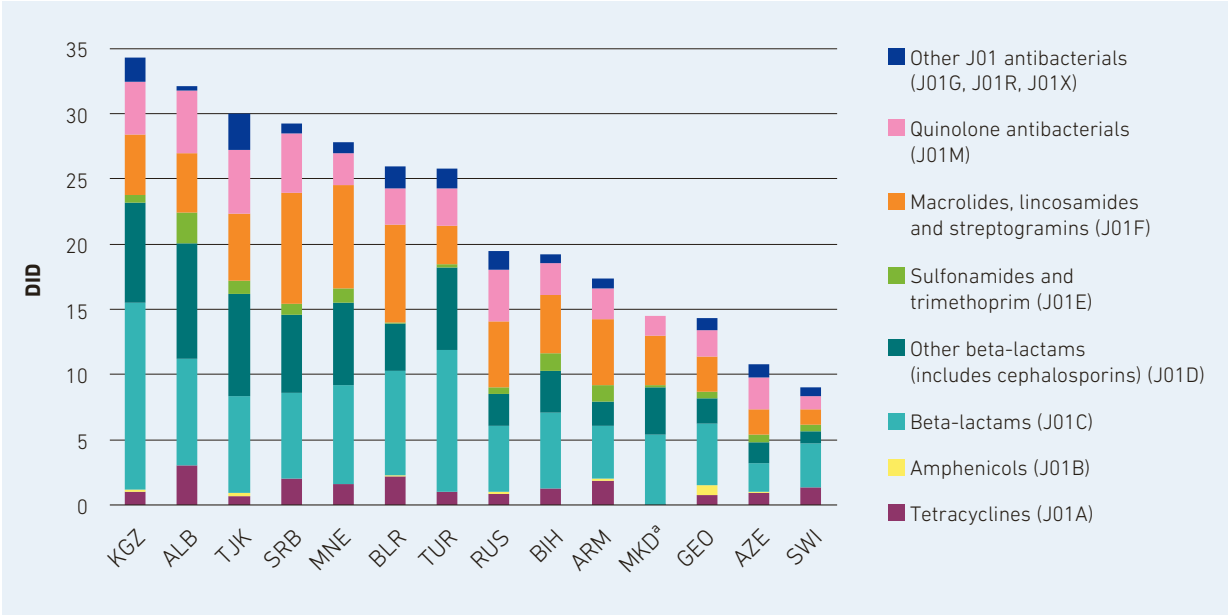
3.1.6 Pharmacological subgroups in 2020

Total consumption of antibacterials for systemic use (ATC class J01) in 2020 is examined by pharmacological subgroup (Fig. 3 and Table 9).

There was considerable variation in the extent of consumption of the different pharmacological subgroups across the AMC Network. In 2020, consumption of beta-lactam penicillins (J01C) ranged from 20% of total J01 consumption in Azerbaijan to 42% of J01 consumption in Kyrgyzstan and Türkiye (Table 9). Cephalosporin (J01D) consumption varied from 10% of J01 consumption in Switzerland to 26% in Tajikistan. Quinolone (J01M) consumption varied from 9% in Montenegro to 22% in Azerbaijan.

Consumption of macrolides, lincosamides and streptogramins (J01F) in 2020 ranged from 12% in Switzerland and Türkiye to 29% in Armenia, Belarus, Montenegro and Serbia. The AMC population-weighted consumption was 20%.

Fig. 3 Total consumption of J01 antibacterials by pharmacological subgroup, 2020



[a] Community consumption.

Table 9 Total consumption of J01 antibacterials by pharmacological subgroup, 2020

Class of antibacterial agents	DID (% of total[a])													
	KGZ	TJK	SRB	MNE	BLR	TUR	RUS	BIH	MKD[b]	GEO	ARM	AZE	SWI	WHO/AMC [c]
Tetracyclines (J01A)	1.0 (3)	0.7 (2)	2.0 (7)	1.6 (6)	2.2 (9)	1.0 (4)	0.9 (4)	1.3 (7)	< 0.1 (0)	0.7 (5)	1.9 (11)	1.0 (9)	1.4 (15)	**1.0 (5)**
Amphenicols (J01B)	0.2 (0)	0.2 (1)	–	–	0.1 (0)	–	0.1 (1)	–	–	0.8 (5)	0.1 (1)	0.1 (0)	–	**0.1 (0)**
Beta-lactam penicillins (J01C)	14.4 (42)	7.4 (25)	6.6 (23)	7.6 (27)	8.0 (31)	10.9 (42)	5.1 (26)	5.8 (30)	5.4 (37)	4.8 (33)	4.1 (23)	2.2 (20)	3.4 (38)	**7.0 (32)**
Other beta-lactams (includes cephalosporins) (J01D)	7.6 (22)	7.8 (26)	5.9 (20)	6.3 (23)	3.6 (14)	6.3 (25)	2.4 (12)	3.2 (17)	3.6 (25)	1.9 (13)	1.9 (11)	1.6 (15)	0.9 (10)	**3.9 (18)**
Sulfonamides and trimethoprim (J01E)	0.6 (2)	1.0 (3)	0.8 (3)	1.1 (4)	0.1 (0)	0.2 (1)	0.5 (3)	1.3 (7)	0.1 (1)	0.5 (4)	1.3 (7)	0.6 (6)	0.6 (6)	**0.5 (2)**
Macrolides, lincosamides and streptogramins (J01F)	4.6 (14)	5.2 (17)	8.5 (29)	7.9 (29)	7.5 (29)	3.0 (12)	5.1 (26)	4.5 (23)	3.8 (26)	2.7 (19)	5.0 (29)	1.9 (18)	1.1 (12)	**4.4 (20)**
Quinolone antibacterials (J01M)	4.0 (12)	4.9 (16)	4.6 (16)	2.5 (9)	2.8 (11)	2.8 (11)	3.9 (20)	2.5 (13)	1.5 (10)	2.0 (14)	2.4 (14)	2.4 (22)	1.0 (11)	**3.4 (16)**
Other J01 antibacterials (J01G, J01R, J01X)	1.8 (5)	2.7 (9)	0.8 (3)	0.8 (3)	1.7 (7)	1.5 (6)	1.5 (8)	0.7 (4)	–	0.9 (6)	0.7 (4)	1.0 (9)	0.7 (8)	**1.5 (7)**
Total	34.3	30.0	29.2	27.8	25.9	25.8	19.5	19.2	14.5	14.3	11.2	10.8	9.0	**21.8**

[a] Total amounts and percentages may vary slightly due to rounding. [b] Community consumption. [c] WHO/AMC population-weighted mean for countries of the AMC Network.

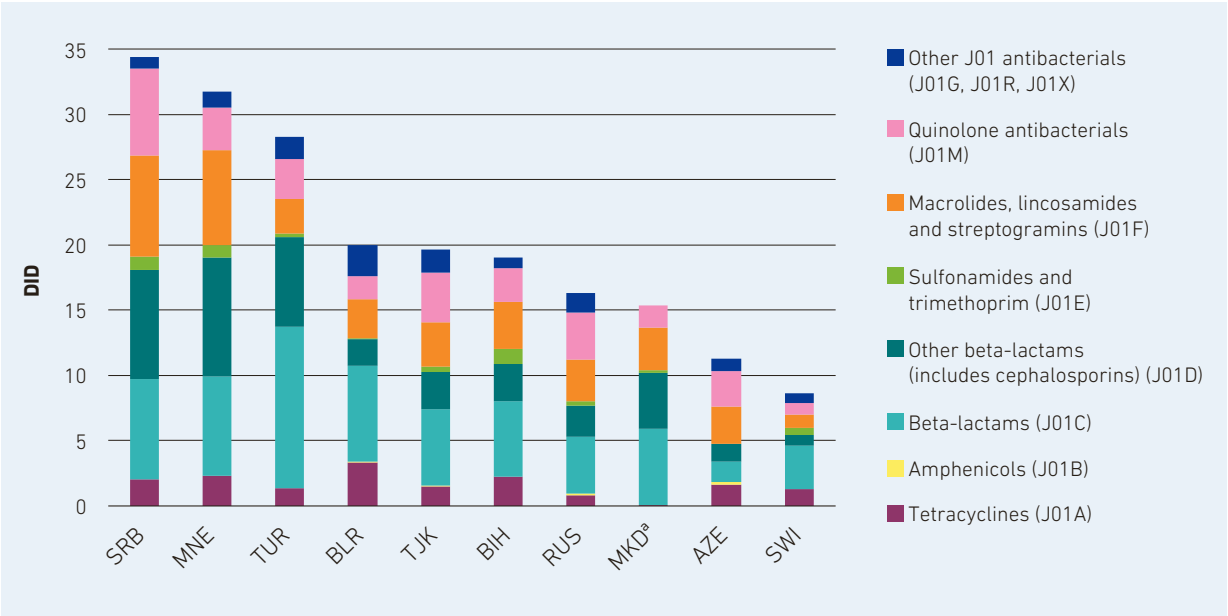
3.1.7 Pharmacological subgroups in 2021

In 2021, consumption of beta-lactam penicillins (J01C) ranged from 14% of total J01 consumption in Azerbaijan to 44% of J01 consumption in Türkiye (Fig. 4 and Table 10). The AMC Network population-weighted mean was 34%.

Cephalosporin (J01D) consumption varied from 10% of J01 consumption in Belarus and Switzerland to 29% in Montenegro. Quinolone (J01M) consumption varied from 9% in Belarus to 24% in Azerbaijan.

Consumption of macrolides, lincosamides and streptogramins (J01F) in 2021 ranged from 10% in Türkiye to 25% in Azerbaijan.

Fig. 4 Total consumption of J01 antibacterials by pharmacological subgroup, 2021



[a] Community consumption.

Table 10 Total consumption of J01 antibacterials by pharmacological subgroup, 2021

Class of antibacterial agents	DID (% of total[a])										
	SRB	MNE	TUR	BLR	TJK	BIH	RUS	MKD[b]	AZE	SWI	WHO/AMC[c]
Tetracyclines (J01A)	2.0 (6)	2.3 (7)	1.3 (5)	3.3 (17)	1.4 (7)	2.2 (12)	0.8 (5)	< 0.1 (0)	1.6 (14)	1.3 (15)	1.2 (6)
Amphenicols (J01B)	–	–	–	< 0.1 (0)	0.1 (1)	–	0.1 (1)	–	0.2 (2)	–	0.1 (0)
Beta-lactam penicillins (J01C)	7.7 (22)	7.6 (24)	12.4 (44)	7.4 (37)	5.8 (30)	5.8 (31)	4.4 (27)	5.8 (38)	1.6 (14)	3.3 (39)	7.0 (34)
Other beta-lactams (includes cephalosporins) (J01D)	8.4 (24)	9.1 (29)	6.8 (24)	2.1 (10)	2.9 (15)	2.8 (15)	2.3 (14)	4.3 (28)	1.4 (12)	0.8 (10)	3.9 (19)
Sulfonamides and trimethoprim (J01E)	1.0 (3)	1.0 (3)	0.3 (1)	0.1 (0)	0.4 (2)	1.1 (6)	0.4 (2)	0.1 (1)	–	0.5 (6)	0.3 (2)
Macrolides, lincosamides and streptogramins (J01F)	7.7 (22)	7.2 (23)	2.7 (10)	3.0 (15)	3.4 (17)	3.6 (19)	3.2 (20)	3.3 (22)	2.8 (25)	1.0 (11)	3.1 (15)
Quinolone antibacterials (J01M)	6.7 (19)	3.3 (10)	3.0 (11)	1.8 (9)	3.8 (19)	2.5 (13)	3.6 (22)	1.6 (11)	2.7 (24)	0.9 (11)	3.3 (16)
Other J01 antibacterials (J01G, J01R, J01X)	0.9 (3)	1.2 (4)	1.7 (6)	2.3 (12)	1.8 (9)	0.8 (4)	1.5 (9)	–	0.9 (8)	0.7 (8)	1.5 (7)
Total	**34.4**	**31.7**	**28.3**	**19.9**	**19.6**	**19.0**	**16.3**	**15.3**	**11.3**	**8.6**	**20.3**

[a] Total amounts and percentages may vary slightly due to rounding. [b] Community consumption. [c] WHO/AMC population-weighted mean for countries of the AMC Network.

3.1.8 Changes in consumption of pharmacological subgroups 2019–2021

Table 11 shows the AMC population-weighted estimates for consumption of pharmacological subgroups in 2019, 2020 and 2021.

The most notable change was the increased relative consumption of the macrolides, lincosamides and streptogramins group (J01F), increasing from 14% of total J01 consumption in 2019 to 20% in 2020 (Table 11). Relative consumption fell towards 2019 levels in 2021 (15%).

The increased consumption of J01F antibacterials is likely to relate in part to their use in diagnosed and presumed COVID-19 infections in 2020. The macrolides group includes azithromycin (J01FA10), which was promoted as a treatment for COVID-19 infection (Oliver & Hinks 2020; Touret et al. 2020). An AMC Network cross-sectional study of supplies of antimicrobials in community pharmacies conducted during the early phases of the pandemic showed that azithromycin was the most supplied agent across a range of clinical indications, not just presumed or confirmed COVID-19 infection (WHO Regional Office for Europe, 2022b).

A United Kingdom-based randomized controlled trial (the PRINCIPLE trial) conducted in primary care settings failed to demonstrate that routine use of azithromycin reduced the time to recovery or the risk of hospitalization for people with suspected COVID-19 in the community (PRINCIPLE Trial Collaborative Group, 2021). This evidence was not published until March 2021. The findings of this trial and other published studies are likely to have contributed to the reduced consumption of azithromycin in 2021.

Table 11 Population-weighted consumption of pharmacological subgroups 2019–2021

Pharmacological subgroup	AMC population-weighted consumption DID (% of total[a])		
	2019	2020	2021
Tetracyclines (J01A)	1.2 (6)	1.0 (5)	1.2 (6)
Amphenicols (J01B)	0.1 (0)	0.1 (0)	0.1 (0)
Beta-lactam penicillins (J01C)	7.5 (35)	7.0 (32)	7.0 (34)
Other beta-lactams (includes cephalosporins) (J01D)	4.4 (21)	3.9 (18)	3.9 (19)
Sulfonamides and trimethoprim (J01E)	0.5 (2)	0.5 (2)	0.3 (2)
Macrolides, lincosamides and streptogramins (J01F)	3.0 (14)	4.4 (20)	3.1 (15)
Quinolone antibacterials (J01M)	3.1 (14)	3.4 (16)	3.3 (16)
Other J01 antibacterials (J01G, J01R, J01X)	1.5 (7)	1.5 (7)	1.5 (7)
Total	**21.2**	**21.8**	**20.3**

[a] Total amounts and percentages may vary slightly due to rounding.

The summary population-weighted estimates of consumption of pharmacological subgroups do not illustrate the variability of changes at country level. Country-level consumption data for J01F antibacterials from 2019 to 2021 are shown in Table 12.

Most countries showed increased relative consumption of J01F antibacterials from 2019 to 2020 and decreases in 2021. However, relative consumption was stable in Türkiye (12% of total J01 consumption in 2019 and 2020, falling to 10% in 2021) and Switzerland (13% in 2019, 12% in 2020, 11% in 2021). In North Macedonia, relative consumption of J01F antibacterials fell in 2020 and then increased in 2021 back to 2019 levels. Consumption of J01F antibacterials continued to increase in Azerbaijan, at 10% relative consumption in 2019, 18% in 2020 and 25% in 2021.

Table 12 Consumption of J01F antibacterials 2019–2021

Year	DID (% of total[a])														
	ARM	AZE	BIH	BLR	GEO	KGZ	MKD[b]	MNE	RUS	SRB	SWI	TJK	TUR	UZB	WHO/AMC[c]
2019	2.1 (19)	1.0 (10)	2.4 (14)	3.1 (14)	2.4 (15)	1.8 (8)	3.4 (22)	5.1 (19)	2.7 (18)	5.6 (21)	1.4 (13)	1.4 (6)	4.1 (12)	3.0 (13)	3.0 (14)
2020	3.8 (26)	1.9 (18)	4.5 (23)	7.5 (29)	5.0 (29)	4.6 (14)	2.7 (19)	7.9 (29)	5.1 (26)	8.5 (29)	1.1 (12)	5.2 (17)	3.0 (12)	–	4.4 (20)
2021	–	2.8 (25)	3.6 (19)	3.0 (15)	–	–	3.3 (22)	7.2 (23)	3.2 (20)	7.7 (22)	1.0 (11)	3.4 (17)	2.7 (10)	–	3.1 (15)

[a] Total amounts and percentages may vary slightly due to rounding. [b] Community consumption. [c] WHO/AMC population-weighted mean for countries of the AMC Network.

3.1.9 Trends, 2014–2021

Table 13 shows the trends in total consumption of antibacterials for systemic use (ATC J01) for the years 2014–2021. 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 at least 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. Countries are grouped according to comparability of data sets.

Ten countries – Azerbaijan, Belarus, Bosnia and Herzegovina, Montenegro, North Macedonia, the Russian Federation, Serbia, Switzerland, Tajikistan and Türkiye – had consumption estimates for all years 2014–2021.

Three of these countries showed statistically significant increases in consumption of J01 antibacterials over the eight years of data collection – Azerbaijan (CAGR +8.4%), Bosnia and Herzegovina (+3.1%) and the Russian Federation (+2.8%). Three countries showed statistically significant reductions in consumption over time – North Macedonia (–0.9%), Switzerland (–3.6%) and Türkiye (–2.9%).

Table 13 Trends in consumption of J01 antibacterials, 2014–2021

Country	Total consumption of J01 antibacterials in DID								CAGR[a]	Trend line	Trend[b]
	2014	2015	2016	2017	2018	2019	2020	2021			–
KAZ	–	17.4	15.7	14.3	15.1	–	–	–	–	–	–
MDA	16.7	12.9	16.7	17.1	14.2	–	–	–	–4.1%		–
UKR	9.5	12.1	8.3	10.7	11.7	–	–	–	5.3%		–
ALB	19.6	16.3	16.5	18.7	19.0	17.2	–	–	–2.6%		–
UZB	–	–	25.1	16.3	18.2	22.2	–	–	–	–	–
ARM	12.7	9.4	9.4	12.0	12.1	11.2	17.4	–	5.3%		–
GEO	17.9	24.2	22.5	25.1	20.8	16.5	14.3	–	–3.7%		–
KGZ	33.1	16.7	21.3	16.9	11.2	21.9	34.3	–	0.6%		–
AZE	6.4	7.4	9.5	7.8	8.9	10.8	10.8	11.3	8.4%		↑
BIH	15.3	16.3	18.0	17.4	19.3	17.4	19.2	19.0	3.1%		↑
BLR	18.3	17.1	16.9	20.0	18.9	22.6	25.9	19.9	1.3%		–
MKD[c]	16.3	16.7	17.0	16.9	16.6	15.6	14.5	15.3	–0.9%		↓
MNE	26.7	29.0	28.9	27.1	27.0	27.1	27.8	31.7	2.5%		–
RUS	13.4	14.1	14.9	15.1	14.7	15.2	19.5	16.3	2.8%		↑
SRB	25.3	31.0	26.2	21.3	22.7	26.6	29.2	34.4	4.5%		–
SWI	11.1	11.1	10.9	10.5	10.7	10.6	9.0	8.6	–3.6%		↓
TJK	31.0	21.7	20.9	16.3	19.0	22.8	30.0	19.6	–6.3%		–
TUR	34.7	35.5	35.3	31.0	30.9	33.2	25.8	28.3	–2.9%		↓

↑↓ indicates statistically significant change.
[a] The CAGR was only calculated where there were five years of data available for the country. [b] Linear regression analysis. [c] Community consumption.

3.2 Relative consumption of AWaRe groups of antibiotics

Analyses based on the WHO AWaRe groups of antibiotics can support antimicrobial stewardship efforts and focus attention on prescribing practices that should be reviewed further.

3.2.1 AWaRe 2020

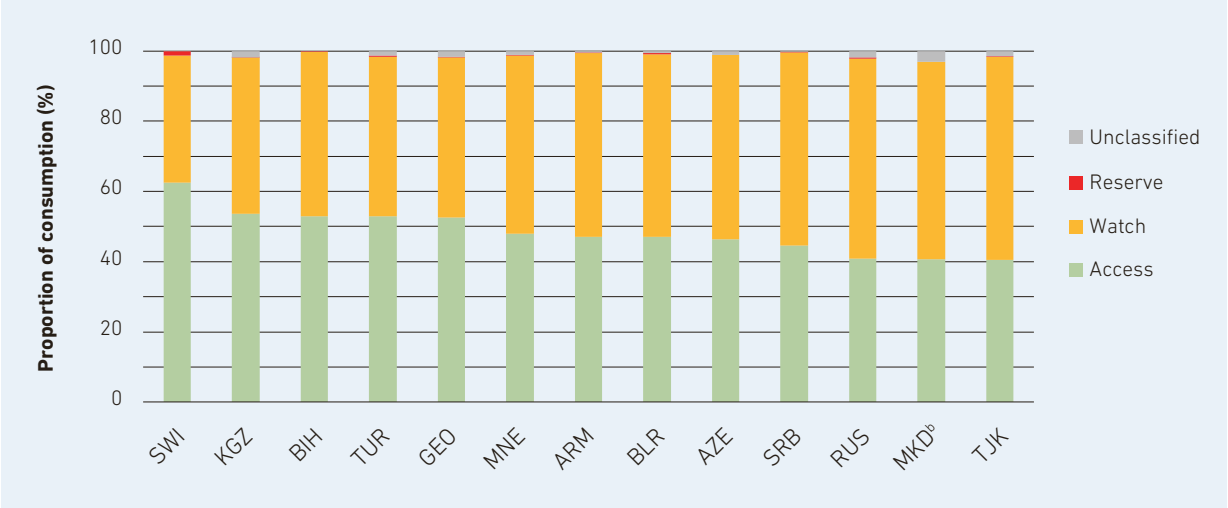
The relative consumption of Access, Watch and Reserve group antibiotics in 2020 is shown in Fig. 5 and is summarized in Table 14.

Consumption of Access agents represented between 41% (North Macedonia, Russian Federation, Tajikistan) and 63% (Switzerland) of total antibacterial consumption in 2020 (Table 14). In 5 of 13 countries (36%), Access agents comprised ≥ 50% of total antibacterial consumption. This compares to 12 of 14 countries (86%) meeting this measure in 2019.

Watch group agents represented between 37% (Switzerland) and 58% (Tajikistan) of total consumption. Consumption of Reserve agents remained low in all 13 countries. Unclassified agents constituted 3% of consumption in North Macedonia and 2% of consumption in Georgia, Kyrgyzstan and the Russian Federation.

The 2020 population-weighted estimates across the AMC Network were: Access agents 46%, Watch agents 52%, Reserve agents 0.2% and unclassified agents 1.5%.

Fig. 5 Relative consumption of antibacterials by WHO AWaRe classification as a proportion of total consumptiona, 2020



[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). [b] Community consumption.

Table 14 Relative consumption of Access, Watch and Reserve classification antibacterials, 2020

Group of antibacterial agents	Consumption according to 2021 WHO AWaRe classification[a]													
	SWI	KGZ	BIH	TUR	GEO	MNE	ARM	BLR	AZE	SRB	RUS	MKD[b]	TJK	WHO/AMC[c]
Access	5.9 (63%)	19.1 (54%)	10.3 (53%)	14.3 (53%)	7.7 (53%)	13.7 (48%)	8.4 (47%)	12.5 (47%)	5.4 (46%)	13.4 (45%)	8.3 (41%)	5.9 (41%)	12.3 (41%)	10.5 (46%)
Watch	3.4 (37%)	15.8 (44%)	9.1 (47%)	12.3 (46%)	6.7 (46%)	14.5 (51%)	9.4 (52%)	13.8 (52%)	6.2 (53%)	16.4 (55%)	11.6 (57%)	8.2 (56%)	17.5 (58%)	11.7 (52%)
Reserve	< 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%)	< 0.1 (0%)	–	< 0.1 (0%)	0.1 (0%)
Unclassified	< 0.1 (0%)	0.7 (2%)	< 0.1 (0%)	0.4 (1%)	0.2 (2%)	0.3 (1%)	0.1 (0%)	0.2 (1%)	0.1 (1%)	0.1 (0%)	0.4 (2%)	0.5 (3%)	0.5 (1%)	0.3 (2%)
Total	**9.3**	**35.5**	**19.5**	**27.0**	**14.6**	**28.5**	**17.9**	**26.6**	**11.7**	**29.9**	**20.3**	**14.6**	**30.3**	**22.6**

[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). [b] Community consumption. [c] Total amounts and percentages may vary slightly due to rounding.

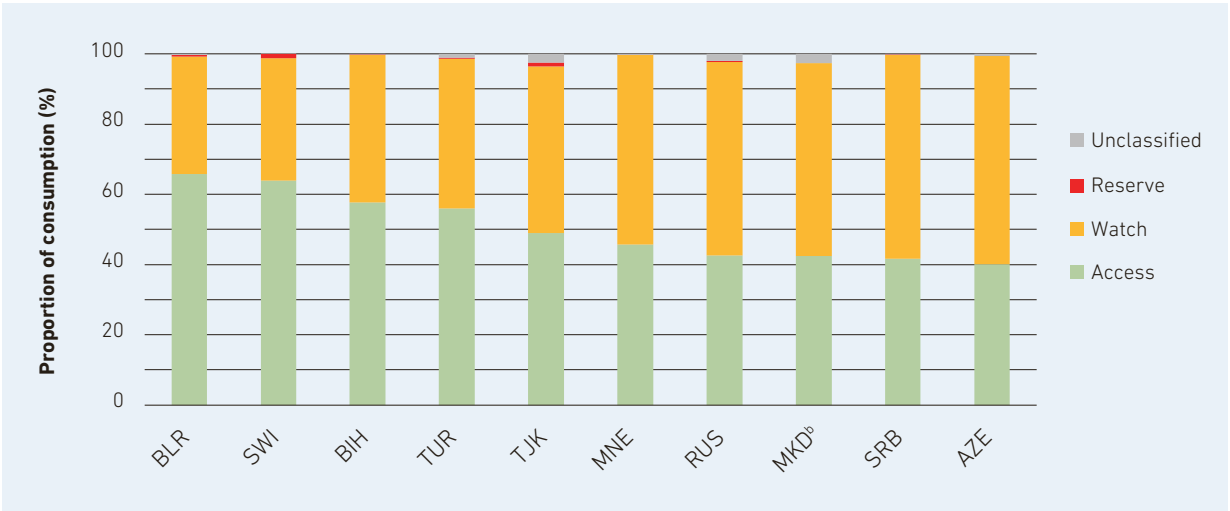
3.2.2 AWaRe 2021

The relative consumption of Access, Watch and Reserve group antibiotics in 2021 is shown in Fig. 6 and is summarized in Table 15.

Consumption of Access agents represented between 40% (Azerbaijan) and 66% (Belarus) of total antibacterial consumption in 2021 (Table 15). In 4 of 10 countries (40%), Access agents comprised ≥ 50% of total antibacterial consumption. By comparison, Watch group agents represented between 33% (Belarus) and 59% (Azerbaijan) of total consumption.

The 2021 population-weighted estimates across the AMC Network were: Access agents 50%, Watch agents 49%, Reserve agents 0.3% and unclassified agents 1.4%.

Fig. 6 Relative consumption of antibacterials by WHO AWaRe classification as a proportion of total consumptiona, 2021



[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). [b] Community consumption.

Table 15 Relative consumption of AWaRe classification antibacterials, 2021

Group of antibacterial agents	Consumption according to 2021 WHO AWaRe classification[a]										
	BLR	SWI	BIH	TUR	TJK	MNE	RUS	MKD[b]	SRB	AZE	WHO/AMC[c]
Access	13.3 (66%)	5.7 (65%)	11.2 (58%)	16.6 (56%)	9.8 (49%)	14.9 (46%)	7.3 (43%)	6.5 (42%)	14.7 (42%)	4.7 (40%)	10.6 (50%)
Watch	6.8 (33%)	3.1 (35%)	8.2 (42%)	12.7 (43%)	9.5 (47%)	17.6 (54%)	9.4 (55%)	8.5 (55%)	20.5 (58%)	7.0 (59%)	10.4 (49%)
Reserve	0.1 (0%)	< 0.1 (0%)	< 0.1 (0%)	0.1 (0%)	0.2 (1%)	< 0.1 (0%)	0.1 (0%)	–	0.1 (0%)	–	0.1 (0%)
Unclassified	0.1 (0%)	< 0.1 (0%)	< 0.1 (0%)	0.3 (1%)	0.5 (2%)	0.1 (0%)	0.3 (2%)	0.4 (3%)	0.1 (0%)	0.1 (1%)	0.3 (1%)
Total	**20.2**	**8.9**	**19.4**	**29.7**	**20.0**	**32.6**	**17.0**	**15.4**	**35.3**	**11.7**	**21.4**

[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). [b] Community consumption. [c] Total amounts and percentages may vary slightly due to rounding.

3.2.3 Changes in AWaRe 2019–2021

WHO/AMC Network population-weighted estimates of the relative consumption of Access, Watch and Reserve classification antibacterials from 2019–2021 are shown in Table 16.

Across AMC Network countries, the relative consumption of Access agents was 50% in 2019, 46% in 2020 and 50% in 2021 (Table 16). Watch group antibiotics constituted 47%, 52% and 49% of total consumption in 2019, 2020 and 2021 respectively. Consumption of Reserve agents and unclassified antibacterials was low in all three years.

Table 16 Relative consumption of AWaRe classification antibacterials, 2019–2021

Group of antibacterial agents	Consumption according to 2021 WHO AWaRe classification[a] WHO/AMC population-weighted estimates DID (% of total[b])		
	2019	2020	2021
Access	11.2 (50%)	10.5 (46%)	10.6 (50%)
Watch	10.3 (47%)	11.7 (52%)	10.4 (49%)
Reserve	< 0.1 (0%)	0.1 (0%)	0.1 (0%)
Unclassified	0.6 (3%)	0.3 (2%)	0.3 (1%)
Total	**22.1**	**22.6**	**21.4**

[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). [b] Total amounts and percentages may vary slightly due to rounding.

3.2.4 WHO global monitoring indicator

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, 2018, 2019). Trends in the relative consumption of Access agents between 2014 and 2019 are shown in Table 17.

Most countries showed patterns like the AMC Network averages, namely decreases in relative consumption of Access agents from 2019 to 2020 and increases in 2021. Russian Federation data indicate a reduction in relative consumption of Access agents from 50% in 2019, to 41% in 2020 and 43% in 2021.

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 17). Only one country, Switzerland, met the WHO target in 2020. This is consistent with the increased consumption of Watch agents in most AMC Network countries in 2020. Two countries, Belarus and Switzerland met the global monitoring target in 2021. No country in the AMC Network met the global monitoring indicator in each of the eight years examined (2014–2021).

Table 17 Countries achieving the target of 60% of total consumption being Access agents, 2014–2021

Country[a]	Access agents as proportion (%) of total consumption[b]							
	2014	2015	2016	2017	2018	2019	2020	2021
ALB	61	48	51	44	40	38	–	–
ARM	67	68	58	66	63	57	47	–
AZE	58	61	50	56	62	71	46	40
BIH	69	69	70	68	66	63	53	58
BLR	57	60	56	62	61	67	47	66
GEO	32	46	60	64	43	54	53	–
KAZ	–	63	60	57	53	–	–	–
KGZ	–	72	56	50	34	54	54	–
MDA	49	56	47	49	51	–	–	–
MKD[c]	53	49	50	48	47	46	41	42
MNE	61	56	58	59	57	60	48	46
RUS	51	51	51	51	50	50	41	43
SRB	68	65	63	60	51	58	45	42
SWI	56	57	59	59	61	62	63	65
TJK	65	58	62	46	43	55	41	49
TUR	45	45	47	48	51	51	53	56
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). [c] Community consumption.

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 (ATC 5th group level). In addition to reporting the numbers of antibacterial agents in the DU75% segment, the agents are categorized according to the AWaRe classification. This facilitates identification of restricted and special use antibacterials that may be widely consumed and be potential targets for stewardship activities.

3.3.1 DU75% 2020

Table 18 (oral agents) and Table 19 (parenteral agents) show the ranking of consumption of antibacterial agents that comprised the DU75% in 2020.

The number of agents constituting the DU75% by oral substance ranged from 5 to 9 across the AMC Network countries (Table 18). There were nine agents in the population-weighted DU75% for the AMC Network.

Azithromycin (J01FA10), a macrolide, was included in the DU75% for 12 of the 13 AMC Network countries and was ranked first most consumed antibiotic in six countries and second in a further five countries. It ranked first in the population-weighted DU75%.

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

Ciprofloxacin (J01MA02), a fluoroquinolone, was included in the DU75% for 9 of the 13 AMC Network countries and was ranked third to fifth most consumed antibiotic in those countries. It ranked fourth in the population-weighted DU75%.

Two to five 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.

The most notable change between 2019 and 2020 was the increased relative consumption of azithromycin – rising from fourth to most consumed oral antibiotic across the AMC Network in 2020.

In 2020, the number of agents constituting the DU75% by parenteral substance ranged from 3 to 10 across the AMC Network countries (Table 19). There were seven agents in the population-weighted DU75%.

The Watch agent ceftriaxone (J01DD04) was ranked number one in nine countries, ranked second in two countries and third in one country. This analysis excludes North Macedonia as only consumption data for oral agents is reported.

Table 18 Ranking of consumption of antibacterials at substance level (ATC 5th level) that comprise the DU75% (oral use), 2020[a]

Agent (ATC)[b]	Ranking of consumption of antibacterial agents that comprised the DU75%													Number of countries[c]	WHO/AMC[d]
	ARM	AZE	BIH	BLR	GEO	KGZ	MKD	MNE	RUS	SRB	SWI	TJK	TUR		
Amoxicillin (J01CA04)	2	3	3	3	7	1		2	2	2	3	1	8	12	3
Amoxicillin and beta-lactamase inhibitor (J01CR02)	4	6	2	2	1	7	1	6	3	3	1		1	12	2
Doxycycline (J01AA02)	3		6	4	6				7	6	2		6	8	5
Sulfamethoxazole and trimethoprim (J01EE01)	5	7	5								5	4		5	9
Nitrofurantoin (J01XE01)		8				8					6		9	4	
Cefalexin (J01DB01)			8					5		5				3	
Metronidazole (P01AB01)		4				6								2	
Tetracycline (J01AA07)		5												1	
Chloramphenicol (J01BA01)					4									1	
Azithromycin (J01FA10)	1	2	1	1	2	2	2	1	1	1	8	2		12	1
Ciprofloxacin (J01MA02)			4		5	3	5	4	5		4	3	4	9	4
Levofloxacin (J01MA12)	6	1		6	3	4			4	7				7	6
Cefixime (J01DD08)						5	3	3	8	4			5	6	8
Clarithromycin (J01FA09)				5			4		6		7		3	5	7
Cefuroxime (J01DC02)			7		8		6						2	4	
Cefaclor (J01DC04)													7	1	
Erythromycin (J01FA01)												5		1	

[a] The antibacterials ranked in this table are grouped by Access agents (green) and Watch agents (yellow). [b] 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). [c] Numbers of countries that have this agent in the DU75%. [d] WHO/AMC population-weighted mean for countries of the AMC Network.

Table 19 Ranking of consumption of antibacterials at substance level (ATC 5th level) that comprise the DU75% (parenteral use), 2020[a]

Agent (ATC)[b]	Ranking of consumption of antibacterial agents that comprised the DU75%												Number of countries[c]	WHO/AMC[d]
	ARM	AZE	BIH	BLR	GEO	KGZ	MNE	RUS	SRB	SWI	TJK	TUR		
Cefazolin (J01DB04)			3			4		4		5		2	5	6
Gentamicin (J01GB03)			2				2		3			10	4	7
Metronidazole (J01XD01)	4		4		2				4				4	5
Ampicillin (J01CA01)						1					2		2	2
Ampicillin and beta-lactamase inhibitor (J01CR01)					6							9	2	
Amoxicillin and beta-lactamase inhibitor (J01CR02)			6							1			2	
Amikacin (J01GB06)					3			5					2	
Flucloxacillin (J01CF05)										6			1	
Ceftriaxone (J01DD04)	1	1	1	1	1	3	1	1	2	2	1	1	12	1
Levofloxacin (J01MA12)	3	2		2	5			2	1		3	6	8	3
Meropenem (J01DH02)			5				3		5			3	4	
Cefotaxime (J01DD01)				3		2		3					3	4
Piperacillin and beta-lactamase inhibitor (J01CR05)										4		5	2	
Moxifloxacin (J01MA14)	2											7	2	
Cefuroxime (J01DC02)										3			1	
Cefepime (J01DE01)				4									1	
Kanamycin (J01GB04)		3											1	
Vancomycin (J01XA01)					4								1	
Teicoplanin (J01XA02)												8	1	
Rifamycin (J04AB03)												4	1	

[a] The antibacterials ranked in this table are grouped by Access agents (green) and Watch agents (yellow). [b] 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). [c] Numbers of countries that have this agent in the DU75%. [d] WHO/AMC population-weighted mean for countries of the AMC Network.

3.3.2 DU75% 2021

Table 20 (oral agents) and Table 21 (parenteral agents) show the ranking of consumption of antibacterial agents that comprised the DU75% in 2021.

The number of agents constituting the DU75% by oral substance ranged from 6 to 8 across the AMC Network countries, with nine agents in the population-weighted DU75% (Table 20).

Oral doxycycline (J01AA02), amoxicillin (J01CA04), amoxicillin and beta-lactamase inhibitor (J01CR02) and azithromycin (J01FA10) were included in the DU75% in 9 of 10 AMC Network countries. Amoxicillin and beta-lactamase inhibitor ranked first for consumption in six of those countries and first in the population-weighted DU75%. Azithromycin was ranked second in the population-weighted DU75%.

Two to five 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.

In 2021, the number of agents constituting the DU75% by parenteral substance ranged from 3 to 10 across the AMC Network countries (Table 21). There were four Access agents and four Watch agents in the population-weighted DU75%.

The Watch agent ceftriaxone (J01DD04) was ranked number one in seven countries and ranked second in a further two countries.

Table 20 Ranking of consumption of antibacterials at substance level (ATC 5th level) that comprise the DU75% (oral use), 2021[a]

Agent (ATC)[b]	Ranking of consumption of antibacterial agents that comprised the DU75%										Number of countries[c]	WHO/AMC[d]
	AZE	BIH	BLR	MKD	MNE	RUS	SRB	SWI	TJK	TUR		
Doxycycline (J01AA02)	4	4	2		6	7	6	2	4	5	9	7
Amoxicillin (J01CA04)	6	3	3	6	1	3	3	3	1		9	3
Amoxicillin and beta-lactamase inhibitor (J01CR02)	3	1	1	1	5	1	4	1		1	9	1
Nitrofurantoin (J01XE01)			5			8		6		7	4	
Sulfamethoxazole and trimethoprim (J01EE01)		6						5			2	
Tetracycline (J01AA07)	5										1	
Ampicillin (J01CA01)									5		1	
Cefalexin (J01DB01)							7				1	
Metronidazole (P01AB01)	7										1	
Azithromycin (J01FA10)	1	2	4	5	2	2	1	7	2		9	2
Ciprofloxacin (J01MA02)		5		4	4	5	8	4	3	3	8	4
Cefixime (J01DD08)				2	3		2			6	4	9
Clarithromycin (J01FA09)		7		3		6				4	4	6
Levofloxacin (J01MA12)	2					4	5		6		4	5
Cefuroxime (J01DC02)			6							2	2	8
Cefaclor (J01DC04)										8	1	

[a] The antibacterials ranked in this table are grouped by Access agents (green) and Watch agents (yellow). [b] 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). [c] Numbers of countries that have this agent in the DU75%. [d] WHO/AMC population-weighted mean for countries of the AMC Network.

Table 21 Ranking of consumption of antibacterials at substance level (ATC 5th level) that comprise the DU75% (parenteral use), 2021[a]

Agent (ATC)[b]	Ranking of consumption of antibacterial agents that comprised the DU75%									Number of countries[c]	WHO/AMC[d]
	AZE	BIH	BLR	MNE	RUS	SRB	SWI	TJK	TUR		
Cefazolin (J01DB04)		2	5		4		6		2	5	3
Metronidazole (J01XD01)	3	5	2		5			4		5	5
Gentamicin (J01GB03)		3		2		3			10	4	8
Amikacin (J01GB06)		4		3				6		3	7
Ampicillin (J01CA01)								2		1	
Flucloxacillin (J01CF05)							5			1	
Ampicillin and beta-lactamase inhibitor (J01CR01)									9	1	
Amoxicillin and beta-lactamase inhibitor (J01CR02)							1			1	
Ceftriaxone (J01DD04)	1	1	1	1	1	2	2	1	1	9	1
Levofloxacin (J01MA12)	2		4		2	1		3	8	6	2
Cefotaxime (J01DD01)			3		3					2	6
Meropenem (J01DH02)			6						3	2	4
Piperacillin and beta-lactamase inhibitor (J01CR05)							4		5	2	
Cefuroxime (J01DC02)							3			1	
Moxifloxacin (J01MA14)									6	1	
Teicoplanin (J01XA02)									7	1	
Rifamycin (J04AB03)									4	1	
Ceftriaxone and beta-lactamase inhibitor (J01DD63)								5		1	

[a] The antibacterials ranked in this table are grouped by Access agents (green) and Watch agents (yellow). [b] 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). [c] Numbers of countries that have this agent in the DU75%. [d] WHO/AMC population-weighted mean for countries of the AMC Network.

3.4 GLASS-IT platform

WHO launched GLASS in 2015 to foster harmonized antimicrobial resistance and use surveillance in all countries and thus inform strategies to contain AMR. GLASS initially focused on surveillance data on human priority bacterial pathogens considered the most significant threat globally. The scope of GLASS has since widened and now incorporates surveillance data on antimicrobial medicines consumption (GLASS-AMC).

WHO has invited AMC Network members to participate in GLASS-AMC. Participation changes the processes for reporting and approval of AMC data. The GLASS-IT platform allows Member States to view their own current and historical AMC data on dedicated country pages.

In addition to the metrics presented in this report, GLASS-AMC reports will also report on:

- Consumption of penicillins (J01CA, J01CE, J01CF and J01CR)
  (quantity of antibiotics as DID, and relative consumption of antibiotics as a percentage of penicillins consumption by chemical subgroups (ATC4))

- Consumption of cephalosporins (J01DB, J01DC, J01DD, J01DE and J01DI)
  (quantity of antibiotics as DID, and relative consumption of antibiotics as a percentage of cephalosporins consumption by chemical subgroups (ATC4))

- Consumption of other antimicrobials groups, namely antimycotics and antifungals
  (quantity of antimycotics and antifungals for systemic use as DID, and relative consumption as a percentage of the consumption of antimycotics and antifungals for systemic use, by chemical subgroups (ATC4)).

The methods for calculation of consumption estimates generally align with those used by the AMC Network. The exception is the population estimates used in the denominator for calculations. The AMC Network applies population estimates from the World Bank, GLASS-AMC uses United Nations population estimates. The impact of this change in source of population data is explored in section 3.4.1.

3.4.1 Source of population data for consumption estimates

Exploratory analyses were conducted using 2021 consumption data to examine the impact of a change in population data source.

The population data for nine countries – Azerbaijan, Belarus, Bosnia and Herzegovina, Montenegro, Russian Federation, Serbia, Switzerland, Tajikistan and Türkiye – were considered in these analyses. In AMC Network reports, national population estimates are applied for Switzerland and Türkiye, rather than World Bank estimates.

Table 22 shows differences in World Bank and United Nations population estimates for the seven countries currently using World Bank population estimates. Results are shown as absolute differences between the estimates and percentages of the World Bank population estimates.

In 6 of the 7 countries, World Bank population estimates were lower than United Nations estimates. The largest differences were Belarus (2.85% lower) and Serbia (7.13% lower).

Table 22 Differences in World Bank and United Nations 2021 population estimates for seven countries

Country	World Bank population estimates	United Nations population estimates	Difference (Word Bank – United Nations)	% difference[a,b]
AZE	10 145 212	10 296 374	−151 162	−1.49%
BIH	3 263 459	3 295 841	−32 382	−0.99%
BLR	9 340 314	9 606 437	−266 123	−2.85%
MNE	620 173	628 205	−8 032	−1.30%
RUS	143 446 060	145 472 994	−2 026 934	−1.41%
SRB	6 844 078	7 331 946	−487 868	−7.13%
TJK	9 749 625	9 643 597	106 028	1.09%

[a] Total amounts and percentages may vary slightly due to rounding. [b] % difference = (World Bank – United Nations)/World Bank*100.

The impact of a change from national estimates to United Nations population statistics for Switzerland and Türkiye is shown in Table 23.

In both cases, national population estimates are higher than United Nations population estimates. The difference is more pronounced in the case of Türkiye, where national population estimates are 4.48% higher than United Nations population estimates.

Table 23 Differences in national and United Nations 2021 population estimates for two countries

Country	National population estimates	United Nations population estimates	Difference (National – United Nations)	% difference[a,b]
SWI	8 738 791	8 670 795	67 996	0.78
TUR	88 417 642	84 459 174	3 958 468	4.48

[a] Total amounts and percentages may vary slightly due to rounding. [b] % difference = (National – United Nations)/World Bank*100

3.4.2 Impact of source of population data on estimates of total consumption of J01 antibacterials

The impact of population data sources on the estimates of total consumption of J01 antibacterials is shown in Table 24.

For 2021, World Bank population estimates were lower than United Nations population estimates in six countries (Table 24). The effect of the use of the lower population estimate is to increase the consumption estimate in DID. The increases are mostly small (< 2%), however in the case of Serbia, application of the World Bank population estimate gives a total consumption estimate 6.7% higher than using the United Nations population estimate.

Table 24 Differences in 2021 total consumption of J01 antibacterials, World Bank and United Nations population estimates, for seven countries

Country	DID[a]			
	Using World Bank population estimates	Using United Nations population estimates	Difference in DID (Word Bank – United Nations)	% difference[b]
AZE	11.27	11.10	0.17	1.47%
BIH	18.99	18.80	0.19	1.00%
BLR	19.95	19.40	0.55	2.77%
MNE	31.70	31.30	0.41	1.28%
RUS	16.26	16.03	0.23	1.39%
SRB	34.38	32.09	2.29	6.65%
TJK	19.63	19.84	-0.22	–1.10%

[a] Total amounts and percentages may vary slightly due to rounding. [b] % difference = (World Bank – United Nations)/World Bank*100

The impact of population data sources on the estimates of total consumption of J01 antibacterials in Switzerland and Türkiye is shown in Table 25. Applying higher national population estimates has the effect of lowering total consumption estimates. The difference is substantial in the case of Türkiye, where application of national population estimates gives an estimate of total consumption of J01 antibacterials that is 4.69% lower than that derived using United Nations population data.

Table 25 Differences in 2021 total consumption of J01 antibacterials, national statistics and United Nations population estimates, for two countries

Country	DID[a]			
	Using national population estimates	Using United Nations population estimates	Difference in DID (National – United Nations)	% difference[a,b]
SWI	8.56	8.62	–0.07	–0.78%
TUR	28.28	29.60	–1.33	–4.69%

[a] Total amounts and percentages may vary slightly due to rounding. [b] % difference = (National – United Nations)/World Bank*100.

These findings are relevant as countries move to AMC consumption calculated using the GLASS-IT platform. Those interpreting and using consumption estimates to inform national policies on access and use of antibiotics need to be aware of the data source used in the calculations, particularly in the situation that historical data based on World Bank population estimates are being compared with new GLASS-AMC estimates. The GLASS-IT platform will recalculate historical data and adjust populations used in the calculations to United Nations estimates, however this can only occur for historical data that are uploaded to the GLASS-IT platform.

When all AMC network members have enrolled in GLASS-AMC, United Nations population estimates will be used in analyses of AMC Network data and reported in any future AMC Network reports. This will ensure consistency in estimates for the AMC Network and GLASS-AMC.

4. DISCUSSION

This report extends the analyses of data from the 2022 AMC Network report (WHO Regional Office for Europe 2022a) 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 2020 (13 AMC Network countries) and 2021 (10 countries).

In 2020, consumption of J01 antibacterials ranged from 9.0 DID (Switzerland) to 34.3 DID (Kyrgyzstan), with median consumption across the 13 countries of 19.5 DID and population-weighted mean consumption of 21.8 DID. The comparable estimates in 2019 ranged from 10.6 DID to 33.2 DID, with a median consumption of 19.6 DID and a population-weighted mean consumption of 21.2 DID.

For the 10 countries with 2021 data, consumption ranged from 8.6 DID (Switzerland) to 34.4 DID (Serbia), with median and population-weighted mean consumption of 19.3 DID and 20.3 DID, respectively.

Analyses of population-weighted consumption estimates across the Network using three years of data, 2019–2021, suggest that there was increased consumption of J01 antibacterials in 2020 and subsequent reductions in consumption in 2021.

The population-weighted pattern of increased consumption from 2019 to 2020 and then a decrease in 2021 was not consistent across all countries. Data from Belarus, Russian Federation and Tajikistan fit this pattern – showing increases in consumption from 2019 to 2020, then falling consumption levels in 2021. However, consumption in Serbia increased in each successive year from 26.6 DID in 2019 to 29.2 DID in 2020 and to 34.4 DID in 2021. In Türkiye, total consumption fell substantially between 2019 and 2020 (33.2 DID to 25.8 DID) before increasing in 2021 to 28.3 DID.

There was considerable variability between countries in the relative consumption of the pharmacological subgroups of J01 antibacterials in both 2020 and 2021. The most notable change over the period 2019–2021 across the Network was the increased relative consumption of the macrolides, lincosamides and streptogramins group (J01F) of agents. The AMC population-weighted estimates showed consumption increasing from 14% of total J01 consumption in 2019 to 20% in 2020, then falling to 15% in 2021.

The same trend of increased antibacterial consumption between 2019 and 2020 was not observed in the European Union/European Economic Area (EU/EEA) countries of the WHO European Region. On the contrary, a significant decrease in antibacterial consumption at the country level was reported by the majority of EU/EEA countries for both the community and hospital sectors. ESAC-Net reported a 17.9% decrease in the EU/EEA population-weighted mean of total antibacterial consumption from 19.9 DID in 2019 to 16.4 DID in 2020 (European Centre for Disease Control, 2021).

A systematic review of data from 20 countries globally showed a reduction in the utilization of health-care services during the COVID-19 pandemic (Moynihan et al., 2021). Reduced provision of health-care services directly impacts patients' access to medicines, including in EU/EEA countries, where access to antimicrobials by prescription is strictly enforced. However, the situation is different in AMC Network countries, where the sale of antimicrobials without a prescription is still prevalent, despite national legislation. A recent study conducted in community pharmacies in nine AMC Network countries during the COVID-19 pandemic found substantial antimicrobial supply occurred without a prescription (WHO Regional Office for Europe, 2022b) This environment, alongside information

widely disseminated about potential treatments for COVID-19, may have partially contributed to the observed increase in antimicrobial consumption in the countries of the AMC Network in 2020.

Increases in consumption in 2020 coincide with the early phases of the COVID-19 pandemic, when several agents were being promoted as potentially useful to reduce hospitalizations and the severity of COVID-19 disease. COVID-19 is a viral infection, so increased use of antiviral agents might have been expected; however, COVID-19 may also be associated with secondary bacterial infections such as pneumonia (Morris et al., 2017). The macrolide antibiotic azithromycin was widely promoted as part of a treatment regimen for COVID-19 (Oliver and Hinks, 2020; Touret et al., 2020). Subsequently, a randomized controlled trial conducted in primary care settings failed to demonstrate that routine use of azithromycin reduced the time to recovery or the risk of hospitalization for people with suspected COVID-19 in the community (PRINCIPLE Trial Collaborative Group, 2021). However, this evidence was not published until March 2021. The findings of this trial and other published studies are likely to have contributed to the reduced consumption of macrolides including azithromycin in 2021. Further investigation at the country level is needed to understand the reasons for the patterns seen and the possible impact of the COVID-19 pandemic on the estimates.

It is also worth noting that many AMC Network countries use import records for national AMC surveillance, which will be a proxy measure of antimicrobial consumption. During the COVID-19 pandemic, global shortages of medicines and health products may have further affected these estimates, leading some countries to increase their imports to prevent potential shortages. As a result, the increases observed in 2020 AMC data which are based on import records, may not necessarily reflect an actual increase in consumption. Therefore, these data should be interpreted within the context of the specific circumstances present in each individual country.

Ten countries had consumption estimates available for all years 2014–2021. Three countries showed statistically significant increases in consumption of J01 antibacterials over the eight years of data collection – Azerbaijan (CAGR +8.4%), Bosnia and Herzegovina (+3.1%) and Russian Federation (+2.8%). Three countries showed statistically significant reductions in consumption over time – North Macedonia (–0.9%), Switzerland (–3.6%) and Türkiye (–2.9%).

AMC Network population-weighted estimates of the relative consumption of Access, Watch and Reserve classification antibacterials from 2019–2021 show that Access agents represented 50% of consumption in 2019, 46% in 2020 and 50% in 2021. Watch group antibiotics constituted 46%, 52% and 49% of total consumption for those same years. Consumption of Reserve agents and unclassified antibacterials was low in all three years. Most countries showed patterns like the Network averages, namely decreases in relative consumption of Access agents from 2019 to 2020 and increases in 2021. This pattern of consumption is likely to be attributable to the increased consumption of Watch group macrolides, including azithromycin, in 2020 and reductions in 2021.

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. Only Switzerland achieved this target in 2020 (63%); Belarus (66%) and Switzerland (65%) met it in 2021.

The number of agents constituting the DU75% – by oral substance – across the AMC Network countries ranged from 5 to 10 in 2020 and 6 to 9 in 2021. There were six Watch agents in the population-weighted DU75% in both years. The most notable change between 2019 and 2020 was the increased relative consumption of azithromycin – rising from fourth to the most consumed oral antibiotic across the AMC Network in 2020. The pattern was consistent, with azithromycin included in the DU75% for 12 of the 13 Network countries in 2020, ranked first most consumed antibiotic in six countries and second in a further five countries.

The scope of WHO's GLASS has widened to include surveillance data on antimicrobial medicines consumption (GLASS-AMC). Network members are transitioning to data collection via the GLASS-IT platform. Analyses are broadly like those conducted by the AMC Network except that GLASS-AMC applies United Nations population estimates for its calculations. Since 2011, the AMC Network has used World Bank population estimates in calculations, apart from Türkiye and Switzerland, where national population estimates are applied. Exploratory analyses were conducted using 2021 consumption data to examine the impact of a change in population data source. In 6 of 7 countries, World Bank population estimates were lower than United Nations estimates, with the largest differences for Belarus (2.85% lower) and Serbia (7.13% lower). For Serbia, the total consumption estimate for 2021 was 6.7% higher using the World Bank population estimate rather than the United Nations population data. For Switzerland and Türkiye, national population estimates are higher than United Nations estimates; 4.48% higher in the case of Türkiye. For Türkiye, use of national population data results in an estimate of total consumption of J01 antibacterials that is 4.69% lower than that derived using United Nations population data.

These findings are relevant as countries move to AMC consumption calculated using the GLASS-IT platform. Those interpreting and using consumption estimates to inform national policies on access and use of antibiotics need to be aware of the data sources used in the calculations, particularly in the situation that historical data based on World Bank population estimates are being compared with new GLASS-AMC estimates. The GLASS-IT platform will recalculate historical data and adjust populations used in the calculations to United Nations population statistics, however this can only occur for historical data that are uploaded to the GLASS-IT platform.

As in previous AMC Network reports, the analyses focus on total consumption of antibacterials. Disaggregation of data to hospital and community sectors is not possible in most Network countries, but this remains an important area for future development as countries strengthen and enhance their surveillance capacity.

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. 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. Further quantitative and qualitative studies conducted in primary care and hospital sectors may be needed to determine reasons for use, as well as doses and duration of treatments prescribed.

Despite some limitations of the data used to estimate antibacterial consumption, it is important that local data are regularly analysed, reviewed and used in decision-making. The quality of the data is unlikely to improve unless the data are seen as relevant and useful for policy development and implementation. Missing information may provide the impetus for commitments to improve the scope and completeness of data collection. Dissemination of information on antibacterial consumption to clinicians and the public will heighten awareness of inappropriate use and problem prescribing and dispensing practices.

Cross-national comparisons in this report allow benchmarking of activities across the AMC Network. Direct comparisons between estimates in 2020 and 2021 are hampered by differences in the countries included in the analyses – 13 countries in 2020 and 10 in 2021. 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.

The transition to data collection and analysis using the GLASS-IT platform should not present significant methodological challenges for AMC Network countries. The information to be collected and analyses conducted are similar to those undertaken in the Network since 2011. When all AMC Network members have enrolled in GLASS-AMC, United Nations population estimates will be used in analyses of AMC Network data and reported in any future AMC Network reports. This will ensure consistency in estimates for the AMC Network and GLASS-AMC, and a common basis for promoting action at the country level and the development of interventions to improve the use of antibacterial agents.

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ANNEX 1. 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

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

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

[a] New addition to EML 2021.

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