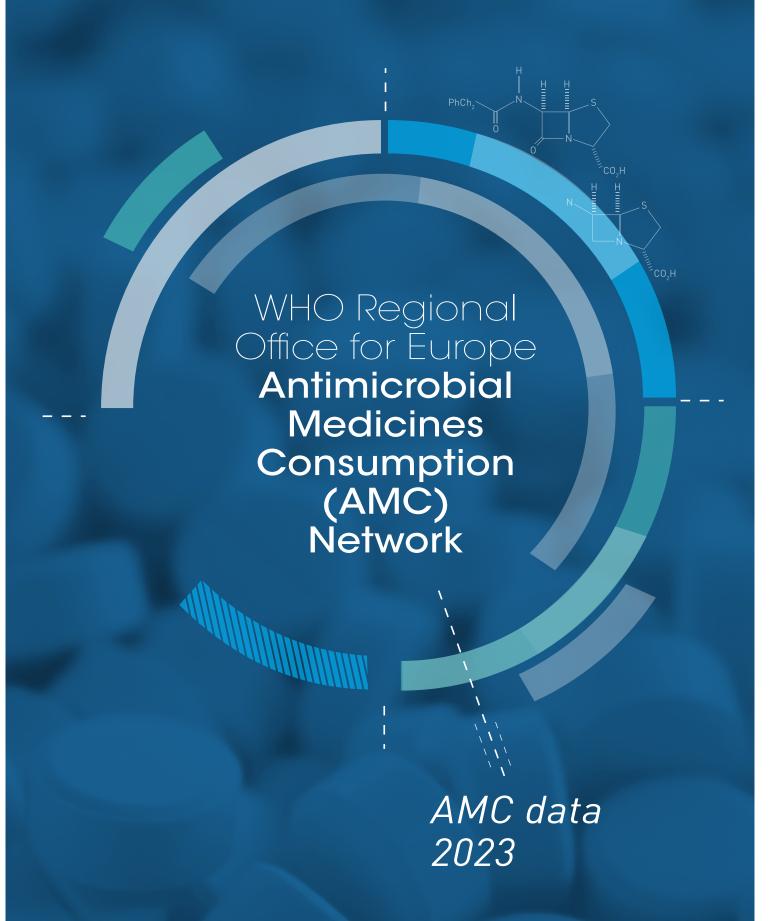


**European Region** 



#### **Abstract**

This report presents analyses of data on antimicrobial medicines consumption collected from non-European Union countries in the WHO European Region – 14 countries provided 2023 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 also examine the consumption of antifungal agents used to treat invasive fungal disease.

#### Keywords

CONSUMPTION
SURVEILLANCE
ANTIBIOTICS
ANTIFUNGALS
RESPONSIBLE USE OF ANTIBACTERIALS
EASTERN EUROPE
CENTRAL ASIA

ISBN: 9789289061872 (PDF)

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

AMC data 2023

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## **ACKNOWLEDGEMENTS**

The WHO Regional Office for Europe would like to thank the following members of the Antimicrobial Medicines Consumption (AMC) Network for providing antimicrobial consumption data and for their valuable contributions to this report.

Mesil Aksoy (Ministry of Health of Türkiye, Turkish Medicines and Medical Devices Agency, Department of Rational Use of Medicines), Marine Baidauri (Regulation Division, Health Care Policy Department, Ministry of Internally Displaced Persons from the Occupied Territories, Labour, Health and Social Affairs of Georgia), Milica Bajčetić (Department of Pharmacology, Clinical Pharmacology and Toxicology, Faculty of Medicine, University of Belgrade, Serbia), Olga Burduniuc (Microbiological Laboratory, National Agency for Public Health, Ministry of Health, Republic of Moldova), Nargis Kalandarova (Department of Conformity Assessment of Medicines of the State Unitary Enterprise for Examination and Testing Pharmaceutical and Medical Products of the Service of State Supervision of Health and Social Protection of Population, Tajikistan), Lidija Cizmovic (Centre for Marketing and Safe Use of Medicines, Institute for Medicines and Medical Devices of Montenegro), Lilith Ghazaryan (Centre of Drug and Medical Technology Expertise of Ministry of Health, Armenia), Irine Gobejishvili (Healthcare Policy Department, Ministry of Internally Displaced Persons from Occupied Territories, Labour, Health and Social Affairs of Georgia), Ihnat Havrylov (Department of Antimicrobial Resistance and Infection Control, Public Health Center, Ministry of Health, Ukraine), Fatma Işli (Ministry of Health of Türkiye, Turkish Medicines and Medical Devices Agency, Department of Rational Use of Medicines), Kristina Hristova (Pharmacy Department, Health Insurance Fund of North Macedonia), Larissa Makalkina (Department of Clinical Pharmacology, Astana Medical University Republican Public Union Professional Association of Clinical Pharmacologists and Pharmacists, Kazakhstan), Fariz Mahmudlu (Analytical Expertise Center's Laboratory of Expertise and Quality Control of Medicines and Pharmaceuticals, Ministry of Health, Azerbaijan), Nazifa Mursalova (Department of Diseases Control, Ministry of Health, Azerbaijan), Mirbek Nyshanbaev (Medicine Registration Unit, Department of Medicines and Medical Devices, Ministry of Health, Kyrgyzstan), Catherine Plüss-Suard (Swiss Center for Antibiotic Resistance, University of Bern, Switzerland), Halina Pyshnik (Organizational and Pharmaceutical Department, Republican Unitary Enterprise "Minsk Pharmacy", Republic of Belarus), Narvina Sinani (National Agency for Drugs and Medical Devices, Albania), Svetlana Rachina (Internal Medicine Department N°2, I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation), Tijana Spasojevic-Dosen (Sector for Providing Information on Drugs and Medical Products, Agency for Medicinal Products and Medical Devices, Bosnia and Herzegovina).

The database for data analysis was developed in conjunction with Public Health Expertise, Paris, France.

The report was written by Jane Robertson and Kotoji Iwamoto of Access to Medicines and Health Products at the WHO Regional Office for Europe.

The activities of the AMC Network are coordinated by the Regional Office. The financial support of the Ministry of Health, Welfare and Sport of the Netherlands (Kingdom of the) and the German Collaboration Programme are gratefully acknowledged.

### **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

COVID-19 coronavirus disease 2019

DDD defined daily dose

DID defined daily doses per 1000 inhabitants per day

DU75% drug utilization 75%

EML WHO Model List of Essential Medicines for adults

EU European Union

GLASS Global Antimicrobial Resistance and Use Surveillance System

IFD invasive fungal disease

IP inhalation powderIS inhalation solution

#### Abbreviations of country names used in tables and figures

ALB Albania MKD North Macedonia ARM Armenia MNE Montenegro

AZE Azerbaijan RUS Russian Federation

BLR Belarus SRB Serbia

BIH SWI Switzerland Bosnia and Herzegovina GEO Georgia TJK Tajikistan Kazakhstan KAZ TUR Türkiye KGZ UKR Ukraine Kyrgyzstan MDA Republic of Moldova UZB Uzbekistan

### **EXECUTIVE SUMMARY**

This is the seventh report of the WHO Regional Office for Europe Antimicrobial Medicines Consumption (AMC) Network. Member States that are currently engaged in the Network 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.

#### **Key findings**

Data on total consumption of antibacterials for systemic use (Anatomical Therapeutic Chemical (ATC) classification group J01) were available for 14 countries. In 2023, consumption ranged from 10.1 defined daily doses per 1000 inhabitants per day (DID) (Ukraine) to 42.7 DID (Türkiye), with a population-weighted mean consumption of 22.2 DID. The comparable estimates for 2022 from 15 countries were 9.6–35.7 DID, with a population-weighted mean of 20.7 DID.

Parenteral formulations represented from 4% to 31% of total consumption of J01 antibacterials. Consumption of beta-lactam penicillins (J01C) ranged from 18% to 46% of total J01 consumption (the AMC Network population-weighted mean was 36%). Cephalosporin (J01D) consumption varied from 9% to 26%, quinolone (J01M) consumption varied from 8% to 20% and consumption of macrolides, lincosamides and streptogramins (J01F) ranged from 9% to 24%.

Three countries showed statistically significant increases in consumption of J01 antibacterials between 2014 and 2023: Azerbaijan (compound annual growth rate (CAGR) +9.5%), Bosnia and Herzegovina (CAGR +4.7%) and Montenegro (CAGR +1.9%). Kazakhstan showed a statistically significant reduction in consumption (CAGR -4.7%) between 2015 and 2023.

Consumption of Access agents ranged from 44% (Ukraine) to 67% (Belarus, Switzerland) of total antibacterial consumption in 2023. Access agents comprised 50% or more of total consumption in nine of 14 countries (64%). In three countries, Watch group agents represented more than half of total consumption: Kazakhstan (53%), the Russian Federation (51%) and Ukraine (52%). Four countries met the target that 60% of all antibiotics consumed should be from the Access group in 2023: Armenia (62%), Belarus (67%), Bosnia and Herzegovina (60%) and Switzerland (67%).

The number of agents constituting the drug utilization 75% (DU75%) by oral substance in 2023 ranged from six to 11 across the 14 AMC Network countries. The Access agents amoxicillin and beta-lactamase inhibitor (ATC code J01CR02) and amoxicillin (J01CA04) ranked first and third, respectively, for consumption in the population-weighted DU75%. The Watch agent azithromycin (J01FA10) was ranked second in the population-weighted DU75%. The Watch agent ceftriaxone (J01DD04) was the most consumed parenteral antibiotic.

Four countries had only one Watch agent in their top five consumed oral antibiotics: Armenia, Belarus, Georgia and Switzerland. There was only one Access agent among the top five agents in North Macedonia and Türkiye.

Consumption data disaggregated by community and hospital sectors were available for six countries – Kazakhstan, Montenegro, the Russian Federation, Switzerland, Türkiye and Ukraine – with community consumption of J01 antibacterials comprising 77–96% of total consumption in 2023. Consumption estimates for North Macedonia are only for the community sector. Most consumption in the community sector was for oral antibacterial agents. Parenteral agents represented 1% to 18% of community consumption. Patterns of community consumption varied across the seven countries. For example, beta-lactam antibacterials (J01C) represented from 22% to 46%, and cephalosporins (J01D) comprised 7% to 25% of community consumption of oral antibiotics.

The substantial differences in patterns of consumption overall and at community level suggest significant differences in management protocols and treatment guidelines at the country level. Reasons for these differences should be investigated, including a review of treatment algorithms and guidelines for common conditions against medicines recommended in the WHO AWaRe antibiotic book and included in the WHO Model List of Essential Medicines.

The number of different agents used to treat invasive fungal disease ranged from one to nine, with total volumes of consumption ranging from 0.114 to 1.087 DID. Parenteral amphotericin was used in 10 countries in low volumes. Fluconazole was the only agent with consumption data in all 14 countries, with consumption ranging from 0.113 to 0.939 DID. Other triazole agents were consumed in low volumes. The echinocandins caspofungin and micafungin were used in eight countries, with very low consumption volumes reported and little change over time.



### 1. INTRODUCTION

#### 1.1 Background

Antimicrobial resistance (AMR) remains a major threat to the sustainability and resilience of health systems, compromising clinical care and affecting the abilities of countries to prepare for and respond to emerging pandemics. The WHO Regional Office for Europe continues to support countries in the WHO European Region to address the challenges of AMR through monitoring and surveillance of resistant bacteria, measuring the consumption of antimicrobials and promoting their prudent use.

The Roadmap on antimicrobial resistance for the WHO European Region 2023–2030 (WHO Regional Office for Europe, 2023) provides guidance to countries on the identification, prioritization, implementation and monitoring of high-impact interventions to tackle 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 AMC in 18 non-European Union (EU) Member States of the Region since 2011 (WHO Regional Office for Europe, 2024). 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, 2024).

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.

Six reports of AMC Network data have been published (WHO Regional Office for Europe, 2017, 2020, 2021, 2022, 2023, 2024). Analyses of AMC Network data have also been presented in the peer-reviewed literature (Robertson et al., 2019, 2021).

#### 1.3 Scope and aim of this report

This report extends the reporting of the AMC Network, presenting 2023 data for 14 Member States that submitted data and gave permission for it to be published.

As in previous reports, crossnational comparisons are presented. Analyses apply the 2023 WHO Access, Watch and Reserve (AWaRe) classification of antibiotics (WHO, 2023) and assess concordance with the WHO global/national target that 60% of total consumption is Access agents (WHO, 2018a). Analyses also report on the antibacterial substances accounting for 75% of consumption – the drug utilization 75% (DU75%) (Zarb et al., 2011). Analyses are also presented on the consumption of antifungal agents used to manage invasive fungal disease (IFD).

### 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 by 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. Details are provided in previous AMC reports (WHO Regional Office for Europe, 2024). In some countries, data are not available for all years examined.

#### 2.1.2 Data collection

Data collection is based on a standardized protocol that is aligned with the *GLASS methodology for surveillance of national antimicrobial consumption* (WHO, 2020) (GLASS stands for Global Antimicrobial Resistance and Use Surveillance System).

#### 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). Only medicines with an assigned ATC code and DDD are included in the analyses.

#### 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. Analyses in this report apply United Nations population estimates for the calculations (UN Population Division, 2024). Exceptions are for Türkiye and Ukraine, where national population estimates are applied, and North Macedonia, where the population eligible for health insurance is used.

#### 2.3 Antimicrobial agents included in this report

#### 2.3.1 Antibacterial agents

The main analyses presented here are for the antibacterials for systemic use (ATC group J01) and related pharmacological subgroups: 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) and other antibacterials (J01X).

Data on additional antibacterials outside the ATC J01 group are also included in the calculation of antibacterial consumption according to the 2023 WHO AWaRe classification (WHO, 2023).

#### 2.3.2 Antifungal agents

There is increasing evidence of antifungal resistance (Fisher et al., 2022). Antifungal resistance can lead to prolonged therapy and hospital stays and can require treatment with expensive second-line antifungal medicines that often are not available in low- and middle-income countries. Consumption analyses are presented in this report for antifungals for the treatment of IFD.

Antifungal agents included in the analyses are:

- antibiotics (polyenes) amphotericin B (J02AA01);
- triazole and tetrazole derivatives fluconazole (J02AC01), itraconazole (J02AC02), voriconazole (J02AC03), posaconazole (J02AC04) and isavuconazole (J02AC05);
- anti-metabolites flucytosine (J02AX01); and
- echinocandins caspofungin (J02AX04), micafungin (J02AX05) and anidulafungin (J02AX06).

#### 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. 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. Estimates are presented separately for community and hospital consumption of antibacterials where possible.

#### 2.4.1.1 Total consumption in DDDs per 1000 inhabitants per day (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, 2018b).

#### 2.4.1.2 Route of administration

Oral administration is generally regarded as the most acceptable and economical method of administration of antimicrobials. This report includes analyses of the use of oral and parenteral formulations for J01 medicines. Consumption of inhalation solution (IS) and inhalation powder (IP) formulations is also reported.

#### 2.4.1.3 Consumption of pharmacological subgroups (ATC 3rd level)

Absolute and relative consumption figures for pharmacological subgroups of J01 and J02 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 of J01 antibacterials was calculated for each participating country. This reflects the average annual change as a proportion (percentage) of the consumption in the starting year. CAGRs were calculated where at least five years of data was available. Linear regression was used to analyse trends in consumption and evaluated using analysis of variance (ANOVA) tests. P values of  $\leq 0.05$  were considered statistically significant.

#### 2.4.3 WHO AWaRe classification

The AWaRe classification (WHO, 2023), first developed in 2017 and updated in 2019, 2021 and 2023, categorizes antibiotics into three groups – Access, Watch and Reserve – considering the impact of different antibiotics and antibiotic classes on AMR to emphasize the importance of their appropriate use. The proportions of consumption (percentage) according to the AWaRe classification are presented in this report.

#### 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, 2018a). The number of countries reaching the WHO global monitoring target in 2023 and across each of the years assessed is reported.

#### 2.4.5 DU75%

The DU75% is calculated for oral and parenteral formulations separately. Results are shown as the ranking of consumption at substance level (ATC 5th level). In addition to reporting the numbers of antibacterial agents in the DU75% segment, the report categorizes the agents in this segment according to the AWaRe classification.

#### 2.4.6 Summary measures applied to crossnational comparisons

AMC Network summary data are presented using population-weighted mean estimates. 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, 2024).

# 3. AMC ACROSS THE AMC NETWORK, 2023

In this chapter, comparisons are made across AMC Network members providing consumption data for 2023 from 14 countries. Where appropriate, comparisons are made with 2022 data (15 countries).

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

#### 3.1.1 Total consumption in 2023

As in previous analyses of AMC Network data, there is wide variability in reported total consumption of J01 antibacterials for systemic use (ATC class J01) for 2023 – ranging from 42.7 DID (Türkiye) to 10.1 DID (Ukraine) (Fig. 1 and Table 1). This compares to a range of 35.7 DID (Türkiye) to 9.6 DID (Armenia) in 2022.

The population-weighted mean total of J01 consumption in 2023 was 22.2 DID, compared to 20.7 DID in 2022.

#### 3.1.2 Route of administration in 2023

The extent of consumption of parenteral formulations varied widely, from 4% in Türkiye up to 31% in Tajikistan (Table 1). North Macedonia data relate to community consumption of oral antibiotics only. There was very low consumption of IS and IP formulations of antibacterials in 2023.

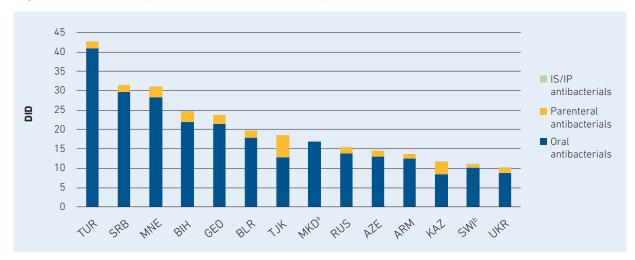


Fig. 1. Total consumption of J01 antibacterials by route of administration in 2023

Table 1. Total consumption of J01 antibacterials by route of administration, 2023

Route of								OID (% c	of total	a)					
administration	TUR	SRB	MNE	BIH	GEO	BLR	TJK	MKDb	RUS	AZE	ARM	KAZ	SWIc	UKR	WHO/AMC <sup>d</sup>
Oral J01	41 (96)	29.6 (94)	28.4 (91)	21.9 (89)	21.4 (90)	17.9 (90)	12.8 (69)	16.8 (100)	13.8 (90)	13 (89)	12.5 (92)	8.4 (73)	10.2 (92)	8.8 (87)	20.4 (91.8)
Parenteral J01	1.7 (4)	1.8 (6)	2.6 (9)	2.8 (11)	2.3 (10)	1.9 (10)	5.7 (31)	-	1.6 (10)	1.5 (11)	1.1 (8)	3.2 (27)	0.8 (8)	1.3 (13)	1.8 (8.1)
IS/IP J01	< 0.01	0.01	< 0.01	0.01	-	-	-	_	0.01 (0.1)	-	-	< 0.01	0.03 (0.3)	0.01 (0.1)	< 0.01
Total	42.7	31.4	31.0	24.7	23.7	19.8	18.4	16.8	15.4	14.5	13.6	11.6	11.0	10.1	22.2

<sup>&</sup>lt;sup>a</sup> Total amounts and percentages may vary slightly due to rounding. <sup>b</sup> Community consumption. <sup>c</sup> Estimates include consumption data of Liechtenstein.

#### 3.1.3 Pharmacological subgroups in 2023

In 2023, consumption of beta-lactam penicillins (J01C) ranged from 18% of total J01 consumption in Azerbaijan and Kazakhstan to 46% of J01 consumption in North Macedonia (Fig. 2 and Table 2). The AMC Network population-weighted mean was 36%.

Cephalosporin (J01D) consumption ranged from 9% of J01 consumption in Switzerland to 26% in Türkiye (the AMC Network population-weighted mean was 20%). Quinolone (J01M) consumption varied from 8% in Belarus and Montenegro to 20% in Kazakhstan and Tajikistan. Consumption of macrolides, lincosamides and streptogramins (J01F) ranged from 9% in Tajikistan to 24% in Serbia.

<sup>&</sup>lt;sup>a</sup> Community consumption. <sup>b</sup> Estimates include consumption data of Liechtenstein.

<sup>&</sup>lt;sup>d</sup> WHO/AMC population-weighted mean for countries of the AMC Network.

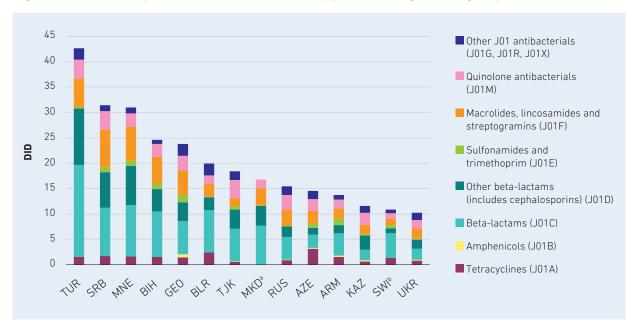


Fig. 2. Total consumption of J01 antibacterials by pharmacological subgroup, 2023

Table 2. Total consumption of J01 antibacterials by pharmacological subgroup, 2023

Classeferente							[	OID (% d	of total	.a)					
Class of agents	TUR	SRB	MNE	BIH	GE0	BLR	TJK	MKDb	RUS	AZE	ARM	KAZ	SWIC	UKR	WHO/AMC <sup>d</sup>
Tetracyclines (J01A)	1.5 (3)	1.7 (5)	1.6 (5)	1.5 (6)	1.4 (6)	2.4 (12)	0.5 (2)	< 0.1	0.9 (6)	3.1 (21)	1.5 (11)	0.6 (5)	1.3 (12)	0.8 (8)	1.1 (5)
Amphenicols (J01B)	-	-	-	-	0.7 (3)	< 0.1	0.1 (1)	-	0.1 (1)	0.2 (2)	0.3 (3)	0.3 (2)	-	0.2 (2)	0.1 (0)
Beta-lactams (J01C)	18.2 (43)	9.5 (30)	10.2 (33)	9 (37)	6.5 (27)	8.4 (43)	6.5 (35)	7.7 (46)	4.5 (29)	2.6 (18)	4.4 (32)	2.1 (18)	4.9 (44)	2.1 (21)	7.9 (36)
Other beta- lactams (includes cephalosporins) (J01D)	11.1 (26)	7 (22)	7.7 (25)	4.4 (18)	3.7 (16)	2.5 (12)	3.8 (21)	3.9 (23)	2 (13)	1.4 (10)	1.6 (12)	2.7 (23)	1 (9)	1.8 (17)	4.5 (20)
Sulfonamides and trimethoprim (J01E)	0.3 (1)	1 (3)	1 (3)	1.1 (5)	1.4 (6)	0.1 (1)	0.6 (3)	0.2 (1)	0.2 (1)	0.8 (5)	1.3 (10)	0.3 (2)	0.6 (6)	0.2 (2)	0.3 (1)
Macrolides, lincosamides and streptogramins (J01F)	5.6 (13)	7.4 (24)	6.7 (22)	5.3 (21)	4.9 (21)	2.6 (13)	1.6 (9)	3.3 (20)	3.2 (21)	2.5 (17)	2 (15)	1.9 (16)	1.3 (12)	2.1 (20)	3.6 (16)
Quinolone antibacterials (J01M)	3.7 (9)	3.7 (12)	2.6 (8)	2.5 (10)	2.9 (12)	1.6 (8)	3.6 (20)	1.7 (10)	2.8 (18)	2.3 (16)	1.7 (12)	2.3 (20)	1 (9)	1.6 (16)	2.8 (13)
Other J01 antibacterials (J01G, J01R, J01X)	2.3 (5)	1.1 (4)	1.2 (4)	0.8 (3)	2.3 (10)	2.3 (11)	1.7 (9)	-	1.7 (11)	1.6 (11)	0.9 (7)	1.4 (12)	0.8 (7)	1.4 (14)	1.8 (8)
Total	42.7	31.4	31	24.7	23.7	19.8	18.4	16.8	15.4	14.5	13.6	11.6	11	10.1	22.2

a Total amounts and percentages may vary slightly due to rounding. b Community consumption. Estimates include consumption data of Liechtenstein.

<sup>&</sup>lt;sup>a</sup> Community consumption. <sup>b</sup> Estimates include consumption data of Liechtenstein.

<sup>&</sup>lt;sup>d</sup> WHO/AMC population-weighted mean for countries of the AMC Network.

#### 3.1.4 Trends 2014-2023

Table 3 shows the trends in total consumption of antibacterials for systemic use (ATC J01) for the years 2014–2023. Thirteen countries – Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Georgia, Montenegro, North Macedonia, the Russian Federation, Serbia, Switzerland, Tajikistan, Türkiye and Ukraine – had consumption estimates for all years.

Three countries showed statistically significant increases in consumption over the ten years of data collection: Azerbaijan (CAGR +9.5%), Bosnia and Herzegovina (CAGR +4.7%) and Montenegro (CAGR + 1.9%). Kazakhstan showed a statistically significant reduction in consumption from 2015–2023 (CAGR -4.7%).

Table 3. Trends in consumption of J01 antibacterials, 2014–2023

		Tot	al cons	umpti	on of J	01 anti	bacter	ials in	DID		0400		<b>-</b> 1b
Country	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	CAGRª	Trend line	Trend <sup>b</sup>
ALB	19.5	16.2	16.3	18.5	18.8	16.9	31.7	-	21.7	-	8.4%		-
ARM	13.1	9.7	9.3	12.0	12.3	11.4	17.7	14.0	9.4	13.6	0.4%	<b></b>	-
AZE	6.4	7.4	9.4	7.8	8.8	10.7	10.7	11.2	14.1	14.5	9.5%		1
BIH	16.3	17.5	18.1	17.7	18.9	17.0	19.0	18.9	21.5	24.7	4.7%		1
BLR	18.3	17.1	17.0	20.0	18.9	22.4	26.0	20.0	16.9	19.8	0.9%		-
GEO	17.6	23.7	22.0	24.6	20.5	16.2	14.0	24.2	19.6	23.7	3.4%	~~~	-
KAZ	-	17.0	15.4	14.0	14.6	11.3	14.0	12.3	10.7	11.6	-4.7%		$\downarrow$
KGZ	33.0	16.7	21.4	17.0	11.3	22.1	34.3	20.6	27.9	-	-2.1%	\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	-
MDA	17.6	13.8	18.2	18.9	15.8	-	-	-	-	-	-2.7%	<u></u>	-
MKDc	16.3	16.7	17.0	16.9	16.6	15.6	14.5	15.3	16.8	16.8	0.4%		-
MNE	26.3	28.7	28.8	27.1	27.2	27.5	28.3	32.5	33.0	31.0	1.9%		1
RUS	13.3	14.0	14.8	14.9	14.5	15.0	19.2	16.0	14.7	15.4	1.6%		-
SRB	24.9	30.5	25.9	21.1	22.5	26.4	29.1	34.2	31.4	31.4	2.6%		-
SWI <sup>d</sup>	11.2	11.3	11.1	10.6	10.8	10.7	9.1	8.7	10.2	11.0	-0.2%		-
TJK	30.5	21.5	20.6	16.0	18.8	22.6	29.6	19.4	16.4	18.4	-5.4%		-
TUR	34.7	35.5	35.4	31.0	30.9	33.2	25.8	28.3	35.7	42.7	2.3%		-
UKR	9.3	11.9	8.6	11.1	12.1	19.4	17.2	12.9	9.7	10.1	0.9%		_
UZB	-	-	25.8	16.7	18.7	22.8	-	-	-	-	-4.0%	<u></u>	-
WHO/ AMC <sup>e</sup>	18.9	19.3	19.8	18.2	18.4	20.5	20.7	18.9	19.9	22.2	1.8%		-

 $<sup>\</sup>uparrow\downarrow$  indicates statistically significant change.

a The CAGR was only calculated where there were five years of data available for the country. Linear regression analysis. Community consumption.

d Estimates include consumption data of Liechtenstein. WHO/AMC population-weighted mean for countries of the AMC Network.

#### 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 2023

The relative consumption of Access, Watch and Reserve group antibiotics in 2023 is shown in Fig. 3 and Table 4.

Consumption of Access agents represented between 44% (Ukraine) and 67% (Belarus and Switzerland) of total antibacterial consumption in 2023 (Table 5). In nine of 14 countries (64%), Access agents comprised 50% or more of total antibacterial consumption. In three countries, Watch group agents represented more than half of total consumption: Kazakhstan (53%), the Russian Federation (51%) and Ukraine (52%).

The 2023 population-weighted estimates across the AMC Network were: Access agents 51% and Watch agents 47%, unchanged from 2022. Reserve and unclassified agents were only a small percentage of consumption.

Fig. 3. Relative consumption of antibacterials by WHO AWaRe classification as a proportion of total consumption, 2023



<sup>&</sup>lt;sup>a</sup> 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). <sup>b</sup> Estimates include consumption data of Liechtenstein. <sup>c</sup> Community consumption.

Table 4. Relative consumption of Access, Watch and Reserve classification antibacterials, 2023

Group of			С	onsum	ption a	ccordir	ng to 20	)23 WH	0 AWa	Re clas	sificati	onª (%	of total	ь)	
agents	BLR	SWI°	ARM	він	AZE	MNE	TJK	TUR	SRB	MKDd	GE0	RUS	KAZ	UKR	WHO/AMC°
Access	13.7 (67)	7.6 (67)	8.8 (62)	15 (60)	8.7 (57)	17.2 (54)	10.1 (54)	23.7 (53)	16.4 (51)	8.3 (49)	11.7 (48)	7.3 (45)	5.3 (45)	4.6 (44)	11.8 (51)
Watch	6.6 (32)	3.7 (33)	5.3 (37)	9.8 (39)	6.4 (41)	14.7 (46)	8.3 (44)	20.6 (46)	15.7 (49)	8 (47)	12 (49)	8.3 (51)	6.3 (53)	5.4 (52)	11 (47)
Reserve	< 0.1	< 0.1	< 0.1	< 0.1	0.1 (1)	< 0.1	< 0.1	0.1 (0)	0.1 (0)	_	0.1 (0)	0.2 (1)	0.1 (1)	< 0.1	0.1 (1)
Unclassified	0.1 (1)	< 0.1	< 0.1	0.3 (1)	0.2 (1)	0.1 (0)	0.4 (2)	0.4 (1)	0.1 (0)	0.6 (4)	0.6 (2)	0.4 (2)	0.1 (1)	0.4 (4)	0.4 (2)
Total	20.5	11.4	14.1	25.1	15.4	32.0	18.8	44.9	32.3	16.9	24.3	16.3	11.8	10.4	23.3

<sup>&</sup>lt;sup>a</sup> 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). <sup>b</sup> Total amounts and percentages may vary slightly due to rounding. <sup>c</sup> Estimates include consumption data of Liechtenstein. <sup>d</sup> Community consumption. <sup>e</sup> WHO/AMC population-weighted mean for countries of the AMC Network.

#### 3.2.2 WHO global monitoring indicator

Trends in the relative consumption of Access agents between 2014 and 2023 are shown in Table 5.

Four countries met the target that 60% of all antibiotics consumed should come from the Access group in 2023: Armenia (62%), Belarus (67%), Bosnia and Herzegovina (60%) and Switzerland (67%). Switzerland is the only country that would have met the target in each of the years since the monitoring indicator was proposed in 2019.

Table 5. Countries achieving the target of 60% of total consumption being Access agents, 2014–2023

			Acce	ss agents a	s proportio	on (%) of to	tal consum	ption <sup>b</sup>		
Country <sup>a</sup>	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
ALB	61	48	51	44	40	37	45	_	39	_
ARM	67	68	58	67	63	57	47	50	51	62
AZE	58	61	50	56	62	71	46	40	50	57
BIH	69	69	70	68	66	63	53	58	62	60
BLR	57	60	56	62	61	67	47	66	68	67
GEO	32	46	60	64	43	54	53	36	42	48
KAZ	-	63	60	57	53	54	42	42	45	45
KGZ	53	72	56	50	34	54	54	61	67	_
MDA	49	56	47	49	51	_	_	_	_	_
MKD°	53	49	50	48	47	46	41	42	48	49
MNE	61	56	58	59	57	60	48	46	51	54
RUS	51	51	51	51	50	50	41	43	45	45
SRB	68	65	63	60	51	58	45	42	49	51
SWI <sup>d</sup>	55	56	58	58	60	61	63	64	66	67
TJK	65	58	62	46	43	55	41	49	48	54
TUR	45	45	47	48	51	51	53	56	54	53
UKR	46	37	51	42	40	34	19	35	40	44
UZB	_	_	31	42	30	35	_	_	_	-
WHO/AMC <sup>e</sup>	50	50	49	50	48	49	44	48	51	51

Country has met the 60% target.

#### 3.3 DU75%

The DU75% represents the antibacterial substances accounting for 75% of consumption measured in DDD and is calculated for oral and parenteral formulations separately. In addition to reporting the numbers and ranking of antibacterial agents in the DU75% segment, the agents are categorized according to the AWaRe classification.

#### 3.3.1 DU75% 2023

The DU75% by oral substance ranged from six to 11 agents across the AMC Network countries (Table 6). There were nine agents in the population-weighted DU75% for the AMC Network.

<sup>&</sup>lt;sup>a</sup> Country estimates are rounded up. <sup>b</sup> 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). <sup>c</sup> Community consumption. <sup>d</sup> Estimates include consumption data of Liechtenstein. <sup>e</sup> WHO/AMC population-weighted mean for countries of the AMC Network.

Two Access group agents were among the five most consumed oral agents. Oral amoxicillin and beta-lactamase inhibitor (ATC code J01CR02) was included in the DU75% in 13 of 14 AMC Network countries, ranked first for consumption in eight of those countries and first in the population-weighted DU75%. Amoxicillin (J01CA04) ranked third in the population-weighted DU75%, appeared in the DU75% for 11 countries and was ranked the most consumed oral antibiotic in three countries.

Watch group antibiotics were ranked in positions two, four and five in the population-weighted DU75% for the AMC Network. Azithromycin (J01FA10), a macrolide, was second in the population-weighted DU75%, included in the DU75% for 12 of the 14 AMC Network countries and was ranked first most consumed antibiotic in three countries.

Ciprofloxacin (J01MA02), a fluoroquinolone, was included in the DU75% for 12 of the 14 AMC Network countries and was ranked fourth in the population-weighted DU75%. Cefixime (J01DD08) was ranked fifth most consumed antibiotic across the Network.

Four countries have only one Watch agent among their top five consumed antibiotics: Armenia, Belarus, Georgia and Switzerland. In three of the four countries, the Watch agent was azithromycin. Ciprofloxacin was the Watch agent in the case of Switzerland, where it was ranked fourth in total consumption.

In contrast, there was only one Access agent, oral amoxicillin and beta-lactamase inhibitor, among the top five agents in North Macedonia and Türkiye. In North Macedonia, the Watch agents cefixime, clarithromycin, ciprofloxacin and azithromycin filled ranks two to five. For Türkiye, the agents ranked in positions two to five were cefuroxime, clarithromycin, ciprofloxacin and cefdinir.

While amoxicillin + enzyme inhibitor, azithromycin and amoxicillin were widely consumed across AMC Network countries, other agents were consumed in volume in only one country: tetracycline (ranked second in Azerbaijan), ampicillin (ranked fifth in Tajikistan) and cefuroxime and cefdinir (ranked second and fifth, respectively, in Türkiye). It is unclear if the observed variations in the patterns of consumption relate to product registration in different countries, differences in the guidelines for the treatment of common conditions in community care, physician prescribing preferences or, in some cases, self-medication by patients.

Furazidin (J01XE03) was the only unclassified agent included in the DU75% for one country, Ukraine.

The Watch agent ceftriaxone (J01DD04) was ranked number one most consumed parenteral antibiotic across 11 of 13 countries (Table 7). This analysis excludes North Macedonia, as only consumption data for oral agents are reported.

Table 6. Ranking of consumption of antibacterials at substance level (ATC 5th level) that comprised the DU75% (oral use), 2023ª

d(OTA)			Rank	ing of co	Ranking of consumption of antibacterial agents that comprised the DU75%	on of an	tibacteri	al agent	s that co	mprised	the DU	,2%			Number of	
Agent (ALC)	ARM	AZE	HH	BLR	GE0	KAZ	MKD	MNE	RUS	SRB	SWIc	¥	TUR	UKR	countries⁴	WHO! AMC
Amoxicillin and enzyme inhibitor (J01CR02)	1	1	1	1	1	7	1	က	2	2	-		1	2	13	1
Doxycycline (J01AA02)	D	വ	נט	က	7	9			7	7	ო		9	က	11	9
Amoxicillin (J01CA04)	2		က	2	6	က		-	_	က	2	-		വ	11	က
Nitrofurantoin (J01XE01)	∞	9		D	D	10			6		9		<sub>∞</sub>	7	6	
Sulfamethoxazole and trimethoprim (J01EE01)	7	<sub>∞</sub>	7		က	6					വ	4			7	6
Cefalexin (J01DB01)								വ		IJ					2	
Metronidazole (J01XD01)		6										9			2	
Tetracycline (J01AA07)		2													1	
Ampicillin (J01CA01)												വ			1	
Azithromycin (J01FA10)	က	4	2	7	2	-	വ	2	က	-		ო		-	12	2
Ciprofloxacin (J01MA02)	9		4		∞	2	4	9	9	9	4	2	4	6	12	4
Cefixime (J01DD08)	7		9		7		2	4	ω	4			7	9	6	വ
Clarithromycin (J01FA09)		7				7	ო		വ				ო	10	9	7
Levofloxacin (J01MA12)		ო			9	2			4	∞				7	9	ω
Cefuroxime (J01DC02)				9		∞					7		2		വ	
Cefdinir (J01DD15)													വ		-	
Furazidin (J01XE03)														œ	-	

Table 7. Ranking of consumption of antibacterials at substance level (ATC 5<sup>th</sup> level) that comprised the DU75% (parenteral use), 2023<sup>a</sup>

			Rankin	g of cons	umption	Ranking of consumption of antibacterial agents that comprised the DU75%	terial ag	ents that	compris	ed the Di	N75%			Number of	
Agent (ATC) <sup>8</sup>	ARM	AZE	BIH	BLR	GE0	KAZ	MNE	RUS	SRB	SWIc	TJK	TUR	UKR	countriesd	WHO/AMC
Metronidazole (J01XD01)	2	2	7	2		4	4	2	က		4		ო	10	က
Cefazolin (J01DB04)			-	4		2			വ	വ	2	2	7	∞	2
Gentamicin (J01GB03)						က	2		2		വ			7	7
Ampicillin and enzyme inhibitor (J01CR01)		7			2							9		ო	
Amikacin (J01GB06)								7	7				വ	ო	7
Ampicillin (J01CA01)											ო			-	
Amoxicillin and enzyme inhibitor (J01CR02)										-				-	
Clindamycin (J01FF01)												∞		-	
Ceftriaxone (J01DD04)	-	-	က	-	-	-	-	-	-	2	-	-	-	13	-
Meropenem (J01DH02)				7	ო				9			က		7	9
Levofloxacin (J01MA12)		က		2				2					2	7	വ
Piperacillin and enzyme inhibitor (J01CR05)					4					4		വ		က	
Cefotaxime (J01DD01)				က				က						2	
Cefepime (J01DE01)				9									9	2	
Vancomycin (J01XA01)							ო		7					2	
Cefuroxime (J01DC02)										т				-	
Streptomycin (J01GA01)					വ									-	
Moxifloxacin (J01MA14)	က													-	
Teicoplanin (J01XA02)												7		-	
Rifamycin (J04AB03)												4		1	
Combinations(J01CE30)			2											1	

<sup>a</sup> The antibacterials ranked in this table are grouped by Access agents and Watch agents. <sup>b</sup> Agents included in this analysis: J01 antibacterials, neomycin (A07AA041), streptomycin (A07AA041), pridaxomicin (A07AA12), rifamycin oral (A07AA13), rifampicin (J04AB02), rifamycin intravenous (J04AB03), rifabutin (J04AB04), metronidazole (P01AB041), finaxomicin (A07AA12), rifamycin oral (A07AA13), rifampicin oral (A07AA013), rifampicin oral (A07AA13), ri

# 3.4 Estimates of volumes of consumption of antibacterials for systemic use (J01) – community

Data disaggregated to community and hospital consumption were available for six countries in 2023: Kazakhstan, Montenegro, the Russian Federation, Switzerland, Türkiye and Ukraine. Results are considered along with consumption estimates for North Macedonia, where data only for the community sector are available.

#### 3.4.1 Community consumption in 2023

Community consumption of J01 antibacterials ranged from 77% of total consumption in Kazakhstan to 96% in Türkiye. (Table 8).

Table 8. Community consumption as a proportion of total consumption of J01 antibacterials, 2023

Setting			D	OID (% of total	a)		
Setting	TUR	MNE	MKD	RUS	SWI⁵	KAZ	UKR
Community J01	41.1 (96)	29.2 (94)	16.8 (100)	13.6 (88)	9.6 (87)	9 (77)	8.9 (88)
Hospital J01	1.6 (4)	1.8 (6)	_	1.8 (12)	1.5 (13)	2.7 (23)	1.2 (12)
Total J01	42.7	31.0	16.8	15.4	11.0	11.6	10.1

<sup>&</sup>lt;sup>a</sup> Total amounts and percentages may vary slightly due to rounding. <sup>b</sup> Estimates include consumption data of Liechtenstein.

#### 3.4.2 Route of administration in 2023

Most consumption in the community sector is for oral antibacterial agents. Parenteral agents represented 1% of community consumption in Türkiye and 18% in Kazakhstan (Table 9).

Table 9. Community consumption of J01 antibacterials by route of administration, 2023

Davita of administration			D	OID (% of total	(a)		
Route of administration	TUR	MNE	MKDb	RUS	SWI°	KAZ	UKR
Oral J01	40.7 (99)	27.9 (96)	16.8 (100)	13 (96)	9.5 (99)	7.4 (82)	8.5 (95)
Parenteral J01	0.4 (1)	1.2 (4)	-	0.6 (4)	< 0.1	1.6 (18)	0.5 (5)
IS/IP	< 0.01 (0)	< 0.01 (0)	-	0.01 (0)	0.02 (0)	-	< 0.01 (0)
Total	41.1	29.2	16.8	13.6	9.6	9.0	8.9

a Total amounts and percentages may vary slightly due to rounding. b Community consumption. Estimates include consumption data of Liechtenstein.

#### 3.4.3 Pharmacological subgroups in 2023

Patterns of consumption in the community varied across the seven countries (Table 10).

Beta-lactam antibacterials (J01C) were the most consumed pharmacological subgroup in all seven countries, ranging from 22% in Ukraine to 46% in North Macedonia. Cephalosporins were widely consumed in Montenegro, North Macedonia and Türkiye (23–25% of community consumption) but less frequently in the Russian Federation and Switzerland (10% and 7% respectively). Agents from the macrolides, lincosamides and streptogramins (J01F) were widely consumed in Montenegro and the Russian Federation (23% of community consumption) and Ukraine (22%). Quinolone antibacterials (J01M) constituted 18% of community consumption in Kazakhstan, but less than 10% of consumption in Montenegro, Switzerland and Türkiye.

Table 10. Community consumption of J01 antibacterials by pharmacological subgroup, 2023

Class of avents				ID (% of total	a)		
Class of agents -	TUR	MNE	MKD	RUS	SWIb	KAZ	UKR
Tetracyclines (J01A)	1.4	1.6	< 0.1	0.8	1.3	0.6	0.8
	(4)	(6)	(0)	(6)	(13)	(7)	(9)
Amphenicols (J01B)	_	_	-	0.1 (1)	-	0.3 (3)	0.2 (2)
Beta-lactams (J01C)	18	10.1	7.7	4.3	4.2	2.1	2
	(44)	(35)	(46)	(32)	(44)	(23)	(22)
Other beta-lactams (includes cephalosporins) (J01D)	10.3	6.7	3.9	1.3	0.6	1.7	1.2
	(25)	(23)	(23)	(10)	(7)	(19)	(14)
Sulfonamides and trimethoprim (J01E)	0.3 (1)	0.9 (3)	0.2 (1)	0.2 (1)	0.6 (6)	0.2 (3)	0.2 (2)
Macrolides, lincosamides and streptogramins (J01F)	5.5	6.6	3.3	3.1	1.2	1.6	2
	(13)	(23)	(20)	(23)	(13)	(18)	(22)
Quinolone antibacterials (J01M)	3.5	2.5	1.7	2.3	0.9	1.6	1.3
	(9)	(9)	(10)	(17)	(9)	(18)	(15)
Other J01 antibacterials	2	0.7	-	1.4	0.7	0.8	1.3
(J01G, J01R, J01X)	(5)	(3)		(10)	(7)	(9)	(14)
Total	41.1	29.2	16.8	13.6	9.6	9	8.9

<sup>&</sup>lt;sup>a</sup> Total amounts and percentages may vary slightly due to rounding. <sup>b</sup> Estimates include consumption data of Liechtenstein.

#### 3.4.4 Trends, 2016-2023

Trends in community consumption of J01 antibacterials between 2016 and 2023 are shown in Table 11. There was a statistically significant increase in community consumption in Montenegro (CAGR +1.2%) and a statistically significant decrease in consumption in Kazakhstan (CAGR -2.8%).

Table 11. Trends in community consumption of J01 antibacterials, 2016-2023

	Со	mmunit	y consui	mption o	of J01 aı	ntibacte	rials in I	DID					
Country	2016	2017	2018	2019	2020	2021	2022	2023	CAGRª	Trend line	Trend⁵		
KAZ	10.9	11.1	11.6	8.5	9.0	8.2	8.2	9.0	-2.8%		$\downarrow$		
MKD	17.0	16.9	16.6	15.6	14.5	15.3	16.8	16.8	-0.2%		-		
MNE	26.9	25.3	25.5	25.7	26.5	30.2	31.3	29.2	1.2%		<b>↑</b>		
RUS	12.6	12.2	12.0	12.8	16.1	13.1	12.7	13.6	1.1%		-		
SWI°	9.5	9.1	9.2	9.1	7.6	7.4	8.8	9.6	0.0%		-		
TUR	34.2	29.8	30.5	31.8	24.4	27.0	34.1	41.1	2.7%		-		
UKR	-	-	-	-	-	11.0	8.8	8.9	-		-		

 $<sup>\</sup>uparrow\downarrow$  indicates statistically significant change.

# 3.5 Estimates of volumes of consumption of antibacterials for systemic use (J01) – hospital

#### 3.5.1 Hospital consumption in 2023

Consumption in the hospital setting was low, varying from 1.2 DID in Ukraine to 2.7 DID in Kazakhstan and representing between 4% (Türkiye) and 23% (Kazakhstan) of J01 consumption in 2023 (Table 8).

#### 3.5.2 Route of administration in 2023

Hospital consumption is dominated by parenteral formulations, which constitute from 54% of consumption in Switzerland to 83% in Türkiye (Table 12).

Table 12. Hospital consumption of J01 antibacterials by route of administration, 2023

Route of			DID (% c	of total <sup>a</sup> )		
administration	KAZ	MNE	RUS	TUR	SWI⁵	UKR
Oral J01	1.1	0.4	0.8	0.3	0.7	0.3
	(42)	(22)	(42)	(17)	(46)	(28)
Parenteral J01	1.6	1.4	1	1.3	0.8	0.8
	(58)	(78)	(58)	(83)	(54)	(71)
IS/IP	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01
	(0)	(0)	(0)	(0)	(0)	(1)
Total	2.7	1.8	1.8	1.6	1.5	1.2

<sup>&</sup>lt;sup>a</sup> Total amounts and percentages may vary slightly due to rounding. <sup>b</sup> Estimates include consumption data of Liechtenstein.

<sup>&</sup>lt;sup>a</sup> The CAGR was only calculated where there were five years of data available for the country. <sup>b</sup> Linear regression analysis. <sup>c</sup> Estimates include consumption data of Liechtenstein.

#### 3.5.3 Pharmacological subgroups in 2023

Patterns of consumption in the hospital setting varied across the six countries (Fig. 4, Table 13). Beta-lactam antibacterials (J01C) were the most consumed pharmacological subgroup in Switzerland (45% of hospital consumption) but represented 5–14% of consumption in the other five countries. Cephalosporins were widely consumed, representing 54% of consumption in Montenegro and 50% in Türkiye, while the lowest was in Switzerland (28%). Quinolone antibacterials (J01M) constituted 27% of hospital consumption in Kazakhstan and the Russian Federation and 21% in Ukraine, but only 5–10% of consumption in the other three countries.



Fig. 4. Hospital consumption of J01 antibacterials by pharmacological subgroup, 2023

<sup>&</sup>lt;sup>a</sup> Estimates include consumption data of Liechtenstein.

Table 13. Hospital consumption of J01 antibacterials by pharmacological subgroup, 2023

Class of amounts			DID (% c	of total <sup>a</sup> )		
Class of agents	KAZ	MNE	RUS	TUR	SWIb	UKR
Tetracyclines (J01A)	< 0.1 (1)	< 0.1 (2)	< 0.1 (2)	< 0.1 (2)	0.1 (3)	< 0.1 (2)
Amphenicols (J01B)	< 0.1 (0)	-	< 0.1 (0)	-	-	< 0.1 (0)
Beta-lactams (J01C)	0.1 (5)	0.1 (7)	0.1 (8)	0.2 (14)	0.7 (45)	0.1 (9)
Other beta-lactams (includes cephalosporins) (J01D)	1 (35)	1 (54)	0.7 (37)	0.8 (50)	0.4 (28)	0.5 (46)
Sulfonamides and trimethoprim (J01E)	< 0.1 (1)	< 0.1 (1)	< 0.1 (1)	0.1 (3)	< 0.1 (2)	< 0.1 (3)
Macrolides, lincosamides and streptogramins (J01F)	0.2 (8)	0.1 (6)	0.1 (5)	0.1 (7)	0.1 (7)	0.1 (8)
Quinolone antibacterials (J01M)	0.7 (27)	0.1 (5)	0.5 (27)	0.2 (10)	0.1 (7)	0.3 (21)
Other J01 antibacterials (J01G, J01R, J01X)	0.6 (23)	0.5 (25)	0.3 (19)	0.2 (14)	0.1 (6)	0.1 (10)
Total	2.7	1.8	1.8	1.6	1.5	1.2

<sup>&</sup>lt;sup>a</sup> Total amounts and percentages may vary slightly due to rounding. <sup>b</sup> Estimates include consumption data of Liechtenstein.

#### 3.5.4 Trends, 2016-2023

Trends in hospital consumption of J01 antibacterials between 2016 and 2023 are shown in Table 14. There were decreases in CAGR in four countries and an increase in one country over the seven-year period examined. However, none of the results were statistically significant.

Table 14. Trends in hospital consumption of J01 antibacterials, 2016–2023

Country	ŀ	lospital	consum	ption of	J01 ant	ibacteri	als in DI	D	CACDa	Torond Days	Torredb
Country	2016	2017	2018	2019	2020	2021	2022	2023	CAGRª	Trend line	Trendb
KAZ	3.1	2.9	3.0	2.8	5.1	4.0	2.5	2.7	-1.8%		-
MNE	1.9	1.8	1.7	1.8	1.8	2.3	1.7	1.8	-0.4%		-
RUS	2.2	2.7	2.5	2.2	3.1	2.9	2.0	1.8	-2.8%		-
SWI°	1.5	1.6	1.6	1.6	1.5	1.3	1.4	1.5	-0.6%		-
TUR	1.1	1.1	0.5	1.3	1.4	1.3	1.6	1.6	5.1%		-
UKR	-	-	-	-	-	1.9	0.9	1.2	_	<u> </u>	_

 $<sup>\</sup>uparrow\downarrow$  indicates statistically significant change.

<sup>&</sup>lt;sup>a</sup> The CAGR was only calculated where there were five years of data available for the country. <sup>b</sup> Linear regression analysis. <sup>c</sup> Estimates include consumption data of Liechtenstein.

### 4. ANTIFUNGAL AGENTS

# 4.1 Estimates of volumes of consumption of antifungals for invasive fungal disease (IFD)

#### 4.1.1 Total consumption of antifungals for IFD in 2023

The number of different agents used to treat IFD ranged from one (Tajikistan) to nine (Belarus and Switzerland), with total volumes of consumption ranging from 0.114 DID (North Macedonia) and 0.116 DID (Bosnia and Herzegovina) to 1.087 DID in Azerbaijan (Fig. 5, Table 15). Parenteral amphotericin B was used in 10 countries, although consumption volumes were low. Fluconazole was the only agent with consumption data in all 14 countries, with consumption ranging from 0.113 DID (Bosnia and Herzegovina, North Macedonia) to 0.939 DID in Azerbaijan. Two other triazoles, itraconazole and voriconazole, were consumed in 11 countries, although in much lower volumes. The echinocandins caspofungin and micafungin were used in eight countries, with very low consumption volumes reported. No country reported consumption of the antimetabolite flucytosine in 2023.

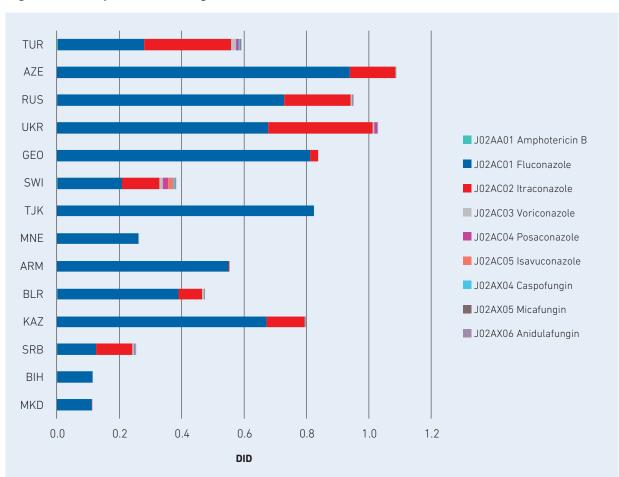


Fig. 5. Consumption of antifungals for IFD, 2023

Table 15. Consumption of antifungals for IFD, 2023

Agent	Š					cons	consumption of antifungals for systemic use in DID	antirunga	S ror syste	emic use ir	מוחנ				
ATC	countries	TUR	AZE	RUS	UKR	GE0	SWIª	ΑŢ	MNE	ARM	BLR	KAZ	SRB	BIH	MKD
Invasive fungal disease															
Antibiotics (polyenes)															
Amphotericin B J02AA01	10	0.004	I	0.001	< 0.001	< 0.001	0.002	1	0.000	I	0.002	< 0.001	0.001	0.001	I
Triazole and tetrazole derivatives															
Fluconazole J02AC01	14	0.275	0.939	0.728	0.677	0.812	0.207	0.824	0.262	0.551	0.388	0.672	0.126	0.113	0.113
Itraconazole J02AC02		0.280	0.147	0.212	0.335	0.025	0.119	I	I	0.002	0.075	0.123	0.115	I	0.002
Voriconazole J02AC03		0.016	0.001	0.005	0.004	0.001	0.011	I	0.002	I	900.0	0.001	0.005	0.001	I
Posaconazole J02AC04	7	0.008	I	0.002	0.010	I	0.018	I	I	I	< 0.001	< 0.001	0.003	I	I
Isavuconazole J02AC05	2	I	I	I	I	I	0.017	I	I	ı	< 0.001	ı	I	I	I
Echinocandins															
Caspofungin J02AX04	∞	0.004	< 0.001	0.001	0.001	I	0.005	I	I	I	0.001	0.001	0.002	I	ı
Micafungin J02AX05	∞	0.003	I	0.001	< 0.001	I	< 0.001	I	I	< 0.001	< 0.001	< 0.001	0.002	I	I
Anidulafungin J02AX06	വ	0.002	I	< 0.001	I	I	0.003	I	I	I	< 0.001	I	0.001	I	I
No. agents consumed		œ	4	œ	7	7	6	1	က	က	6	7	80	က	2
Total DID <sup>c</sup> in 2023		0.592	1.087	0.950	1.028	0.838	0.383	0.824	0.263	0.552	0.474	0.797	0.254	0.116	0.114

<sup>a</sup> Estimates include consumption data of Liechtenstein. <sup>b</sup> Community consumption. <sup>c</sup> Total amounts and percentages may vary slightly due to rounding.

#### 4.1.2 Trends 2019-2023

Thirteen of 14 countries had estimates of consumption for IFD for the five-year period 2019 to 2023 (Table 16). Due to the sparseness of data and low levels of consumption for some agents, the CAGR of total antifungal consumption was not calculated.

Parenteral amphotericin B was used in eight to ten countries across the five years of data, with low levels of consumption. There was evidence of a small increase in the consumption of fluconazole across the network from 2019 to 2023. There were no substantial changes in the consumption of the echinocandins over the five years.

Table 16. Population-weighted mean consumption (DID) of antifungals for IFD across 13 countries, 2019–2023

ATC	(N	Population- o. countries repo	and the second s	n consumption sumption of th		
	Agent	2019	2020	2021	2022	2023
Antibiotics (polyenes)						
J02AA01	amphotericin B (parenteral)	0.008	0.007 (9)	0.012 (9)	0.01 (8)	0.002 (10)
Triazole and tetrazole	e derivatives					
J02AC01	fluconazole	0.487 (15)	0.583 (15)	0.45 (14)	0.499 (14)	0.566 (14)
J02AC02	itraconazole	0.254 (11)	0.152 (10)	0.149 (11)	0.156 (10)	0.215 (11)
J02AC03	voriconazole	0.02 (9)	0.006 (10)	0.043 (9)	0.044 (11)	0.007 (11)
J02AC04	posaconazole	0.003 (6)	0.003 (6)	0.004 (5)	0.004 (5)	0.004 (7)
J02AC05	isavuconazole	< 0.001 (1)	< 0.001 (1)	< 0.001 (2)	< 0.001 (2)	< 0.001 (2)
Antimetabolites						
J02AX01	flucytosine	< 0.001 (1)	< 0.001 (1)	< 0.001 (1)	-	-
Echinocandins						
J02AX04	caspofungin	0.001 (6)	0.002 (6)	0.002 (5)	0.002 (6)	0.002 (8)
J02AX05	micafungin	0.001 (7)	0.001 (8)	0.001 (6)	0.001 (7)	0.001 (8)
J02AX06	anidulafungin	0.001 (4)	0.001 (4)	0.001 (5)	0.001 (5)	0.001 (5)

### 5. DISCUSSION

The analyses in this report are mostly crossnational comparisons of consumption data for 2023 from 14 AMC Network countries. Primary analyses relate to J01 antibacterials, where consumption patterns mirror the variability shown in earlier reports. Total consumption ranged from 10.1–42.7 DID in 2023 compared to 9.6–35.7 DID from 15 countries in 2022. The population-weighted mean consumption across the Network was 22.2 DID in 2023 (20.7 DID in 2022). Relative consumption of parenteral formulations varied widely (range 4–31% of total consumption) as did patterns of consumption of pharmacological subgroups.

Thirteen countries had consumption estimates available for all years from 2014 to 2023. Three countries showed statistically significant increases in consumption of J01 antibacterials over this period: Azerbaijan (CAGR +9.5%), Bosnia and Herzegovina (CAGR +4.7%) and Montenegro (CAGR + 1.9%). Kazakhstan showed a statistically significant reduction in consumption (CAGR -4.7%) between 2015 and 2023. The extent to which the coronavirus disease 2019 (COVID-19) pandemic has affected these trends is unclear. Analyses of data reported to the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) showed a significant decrease in antibiotic consumption in the community sector of EU/European Economic Area countries coincident with the first year of the COVID-19 pandemic. However, the decreases appear to have been transient with consumption back at pre-pandemic levels in 2022 (Ventura-Gabarró et al, 2023) and further increases in some countries in 2023, such that the EU population-weighted mean total consumption (community and hospital sectors combined) of J01 antibacterials was 1% higher than in 2019 (European Centre for Disease Prevention and Control, 2024). Further work is needed to understand patterns of antibiotic consumption pre- and post-COVID-19 pandemic in AMC Network countries.

Consumption of Access agents ranged from 44% (Ukraine) to 67% (Belarus, Switzerland) of total antibacterial consumption in 2023. Access agents comprised 50% or more of total consumption in nine of 14 countries (64%). In three countries, Watch group agents represented more than half of total consumption: Kazakhstan (53%), the Russian Federation (51%) and Ukraine (52%). Four countries met the target that 60% of all antibiotics consumed should be from the Access group in 2023: Armenia (62%), Belarus (67%), Bosnia and Herzegovina (60%) and Switzerland (67%).

The number of agents constituting the DU75% by oral substance in 2023 ranged from six to 11 across the 14 AMC Network countries. Four countries have only one Watch agent in their top five consumed antibiotics: Armenia, Belarus, Georgia and Switzerland. In three of the four countries, the Watch agent was azithromycin. Ciprofloxacin was the Watch agent in the case of Switzerland, where it was ranked fourth in total consumption.

In contrast, there was only one Access agent, oral amoxicillin and beta-lactamase inhibitor, among the top five agents in North Macedonia and Türkiye. In North Macedonia, the Watch agents cefixime, clarithromycin, ciprofloxacin and azithromycin filled ranks two to five. For Türkiye, the agents ranked in positions two to five were cefuroxime, clarithromycin, ciprofloxacin and cefdinir.

While amoxicillin + enzyme inhibitor, azithromycin and amoxicillin were widely consumed across AMC Network countries, other agents were consumed in volume in only one country: tetracycline (ranked second in Azerbaijan), ampicillin (ranked fifth in Tajikistan) and cefuroxime and cefdinir (ranked second and fifth, respectively, in Türkiye). It is unclear if the observed variations in the patterns of

consumption relate to product registration in different countries, differences in the guidelines for the treatment of common conditions in community care, physician prescribing preferences or, in some cases, self-medication by patients.

Consumption data disaggregated by community and hospital sectors were available for six countries – Kazakhstan, Montenegro, the Russian Federation, Türkiye, Switzerland and Ukraine – with community consumption of J01 antibacterials comprising 77–96% of total consumption in 2023. Consumption estimates for North Macedonia are only for the community sector. Most consumption in the community sector was for oral antibacterial agents. Parenteral agents represented 1% to 18% of community consumption. Patterns of community consumption varied across the seven countries. For example, beta-lactam antibacterials (J01C) represented from 22% to 46%, and cephalosporins (J01D) comprised 7% to 25% of community consumption of oral antibiotics.

The substantial differences in patterns of consumption overall and at community level suggest significant differences in management protocols and treatment guidelines at the country level. Reasons for these differences should be investigated, including a review of treatment algorithms and guidelines for common conditions against medicines recommended in the *WHO AWaRe antibiotic book* (WHO, 2022a, 2022b) and included in the 2023 WHO Model List of Essential Medicines (EML) (WHO, 2023).

The number of different agents used to treat IFD ranged from one to nine, with total volumes of consumption ranging from 0.114 to 1.087 DID. Parenteral amphotericin was used in 10 countries in low volumes. Fluconazole was the only agent with consumption data in all 14 countries, with consumption ranging from 0.113 to 0.939 DID. Other triazole agents were consumed in low volumes. The 2022 WHO priority fungal agents report (WHO, 2022c) noted that, while existing antifungal medicines are effective, they are associated with a range of adverse effects, lengthy courses of treatment and drug–drug interactions. Additionally, affordable access to quality medicines and diagnostic tests is unevenly distributed, meaning that many fungal infections go undiagnosed and untreated. To promote attention to the problems of managing IFD and increasing antifungal resistance, the echinocandin micafungin was added to the complementary list of the WHO EML in 2021 with a square-box listing, nominating anidulafungin and caspofungin as alternatives. Consumption data for caspofungin and micafungin were reported in 2023 from eight countries, however, with very low consumption volumes. There was little evidence of increases in consumption or the numbers of countries reporting use of the echinocandins between 2019 and 2023, despite their inclusion in the WHO EML.

As noted in previous analyses, the limitations of some of the data have implications for the interpretation of results. Only medicines with an assigned ATC code and DDD are included in the analyses. Where medicines without codes are 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 indications for treatment, some results are difficult to interpret. A fuller interpretation of the consumption data requires an understanding of the local context.

These limitations do not diminish the importance of regular analysis of local data, its dissemination to relevant health-care professionals and communities and its use to inform decision-making. The quality of the data is unlikely to improve unless the data are seen as relevant, timely and useful for policy development and implementation. Missing information may provide the impetus for commitments to improve the scope and completeness of data collection. The dissemination of information on antibacterial consumption to clinicians and the public will heighten awareness of inappropriate use and problem prescribing and dispensing practices. Substantial differences in the volumes and patterns of consumption between countries that have been reported in consecutive AMC Network reports suggest there are many targets for further studies, both quantitative and qualitative, to understand better the use of these medicines in clinical practice.

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