World Health Organization

European Region

Antimicrobials supplied in community pharmacies

in eastern Europe and central Asia in the early phases of the COVID-19 pandemic

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Abstract

During the COVID-19 health crisis, community pharmacists had an enhanced role in supporting health-care systems that were overburdened by managing seriously ill patients. This study was undertaken to determine the patterns of community supply of antiviral and antibacterial agents from community pharmacies during the COVID-19 pandemic in selected countries in eastern Europe and central Asia. Nine countries – Armenia, Georgia, Kazakhstan, Kyrgyzstan, North Macedonia, the Russian Federation, Serbia, Tajikistan and Uzbekistan – participated in this cross-sectional study. Country reports include the results of national and regional analyses conducted. The results of the crossnational analyses presented in this report supplement country reports and can be used to review issues around access to, and appropriate choices of, antibacterial agents for common presentations in community care.

Keywords

ANTIMICROBIAL MEDICINES
ANTI-INFECTIVE AGENTS – THERAPEUTIC USE
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ACRONYMS

ATC	Anatomical Therapeutic Chemical (categories)
AWaRe	(WHO) Access, Watch, Reserve (classification)
CHMP	Committee for Medicinal Products for Human Use (of the European Medicines Agency)
EMA	European Medicines Agency
ICD-10	International Classification of Diseases and Related Health Problems 10th Revision
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
URTI	upper respiratory tract infection
UTI	urinary tract infection
WHO HREC	WHO Human Research Ethics Committee

EXECUTIVE SUMMARY

During the COVID-19 health crisis, community pharmacists had an enhanced role in supporting health-care systems, providing advice to customers on the management of their symptoms and treatments for other acute and chronic medical conditions. Using a common protocol, studies were undertaken in nine countries in eastern Europe and central Asia – Armenia, Georgia, Kazakhstan, Kyrgyzstan, North Macedonia, the Russian Federation, Serbia, Tajikistan and Uzbekistan – to determine the patterns of community supply of antiviral and antibacterial agents from community pharmacies during the COVID-19 pandemic. In all but Serbia, the studies involved data collection from a random sample of community pharmacies from the capital city and several regions outside the capital.

In the eight countries using manual data-collection methods, pharmacists recorded all episodes of supply of antimicrobial agents to customers during a one-week period. Information was obtained on the age and gender of the patient, antimicrobials sold and formulation type, whether supply related to the presentation of a prescription, and the reason for the supply (indication). In Serbia, relevant data were extracted from the health information system that collects data on dispensed medicines in all public and 90% of private community pharmacies. Data related to antimicrobial supplies for 13–19 April 2020 and results were compared to the same week in 2019. The top 10 agents used for the management of upper respiratory tract infection (URTI), urinary tract infection (UTI) and COVID-19 were examined.

Key findings

Across the eight country studies using manual data-collection methods – Armenia, Georgia, Kazakhstan, Kyrgyzstan, North Macedonia, the Russian Federation, Tajikistan and Uzbekistan – 25 843 community pharmacy encounters in which one or more antimicrobials were supplied during the week of data collection were recorded. Data collection ranged from 1220 encounters in 96 pharmacies in Kyrgyzstan to 9818 encounters in 92 pharmacies in Uzbekistan. Only the Russian Federation and Uzbekistan included public pharmacies in their studies.

All countries except Tajikistan and Uzbekistan recorded more encounters with females than males, ranging from 60.2% in the Russian Federation to 53% in North Macedonia. Most encounters related to clients aged 19–60 years. Encounters for customers aged over 60 years ranged from 2.7% in Kyrgyzstan to 26.1% in North Macedonia.

Supply related to presentation of a prescription ranged from 22.7% of encounters in Tajikistan to 97.1% in North Macedonia. A "reason for use" was available for almost all encounters. Oral formulations were the most supplied medicine type, ranging from 56.3% of encounters in Tajikistan to 99.2% in North Macedonia. Highest rates of supply of parenteral formulations were in Kazakhstan (24.5%), Kyrgyzstan (31.9%) and Tajikistan (43.7%).

Across all encounters, Anatomical Therapeutic Chemical (ATC) code J01 antimicrobial agents were most often supplied, representing between 61.9% (the Russian Federation) and 96% (North Macedonia) of all antimicrobials supplied. There was no evidence of differences in formulations of J01 antibacterials supplied to female and male customers, but some evidence suggested differences in formulations supplied according to age, with highest rates of supply of parenteral formulations to

customers aged over 60 years. Only the Russian Federation reported significant numbers of supplies of antiviral agents (ATC code J05, 26.7% of supplies).

URTI was the most recorded indication for treatment in each of the eight country studies, from 32.8% of cases in Uzbekistan to 64.5% in Georgia. A wide variety of oral and parenteral agents was included in the top 10 treatments for URTI. Azithromycin was ranked most supplied agent in five countries and ranked second in three. Oral amoxicillin was in the top 10 agents for all eight countries, with the fluoroquinolones ciprofloxacin and levofloxacin in the top 10 agents for URTI in six and seven countries respectively. Instances of UTI ranged from 8.6% of encounters in Armenia to 25.7% in Georgia. Most supplied agents were J01antibacterials, notably fluoroquinolones, with ciprofloxacin and levofloxacin included in the top 10 agents in all eight countries.

COVID-19-related reasons for supply ranged from 0.5% in Georgia to 15.3% in Armenia. Thirteen oral and eight parenteral agents were included in the top 10 agents across the country studies. Levofloxacin was included in the top 10 in all eight countries; azithromycin was the first-ranked agent in five countries. Hydroxychloroquine was ranked second for supply in Georgia and Uzbekistan. Azithromycin and hydroxychloroquine were suggested early in the pandemic as a possible prevention method or treatment for COVID-19, given evidence of in vitro inhibition of severe acute respiratory syndrome coronavirus 2.

The Serbian health information system provided data on dispensed medicines from 561 public and 3135 private pharmacies. A dramatic reduction in numbers of encounters involving supply of antimicrobials was noted, falling from 91 964 encounters in 2019 to 30 575 for the comparable period in 2020. There were more encounters with females than males, with some differences in age distribution of clients compared to the other country studies. All encounters related to presentation of a prescription; only oral formulations are supplied in community pharmacies. Patterns of supply according to ATC codes and indication (based on International Classification of Diseases and Related Health Problems 10th Revision (ICD-10) codes) were similar to the eight country studies conducted using manual methods. Notably there were fewer instances of URTI reported in 2020 than 2019. ICD-10 codes for COVID-19 were not incorporated into the health information system in Serbia until June 2020, so they were not applied by treating physicians at the time this study was conducted.

Conclusions

These studies illustrate the value of a review of prescribing and dispensing practices, in this case, in the context of the evolving COVID-19 pandemic in 2020. In the absence of electronic systems, manual data-collection methods in community pharmacies can be used to collect information that can inform understanding of how the medicines are used in practice. Overall, the trends were towards increased use of medicines that had been proposed for the treatment for COVID-19 infection, specifically azithromycin and, to a lesser extent, hydroxychloroquine. Azithromycin, however, was the most supplied agent across a range of clinical indications, not just presumed or confirmed COVID-19 infection.

The results of the crossnational analyses presented in this report supplement country-level reports of national data and regional comparisons and can be used to review issues around access to, and appropriate choices of, antibacterial agents for common presentations in community care.

1. BACKGROUND

During the COVID-19 health crisis, community pharmacists had an enhanced role in supporting health-care systems that were overburdened by managing seriously ill patients. Those unwell may have visited pharmacies first, seeking professional advice on the management of their symptoms and treatments for other acute and chronic medical conditions.

As health-care professionals, pharmacists should follow national recommendations for the management of COVID-19 infection, including use of appropriate medicines such as paracetamol and non-steroidal anti-inflammatory drugs for fever. Pharmacists also have a role in countering misinformation and false claims about the effectiveness of some treatments for COVID-19 and should not promote or recommend products of doubtful efficacy.

COVID-19 is a viral infection, so increased use of antiviral agents might be expected. COVID-19 infection may also be associated with secondary bacterial infections such as pneumonia *(1)*. The antibiotic azithromycin has been promoted as part of a treatment regimen for COVID-19. In addition, there is evidence of antibiotics being used to treat the symptoms of viral infections such as upper respiratory tract infections (URTIs) and influenza, despite them not being effective. Several agents were widely discussed in the mainstream media and in social media and it might be expected that demand for, and usage of, these agents would have increased.

This study was undertaken to determine the patterns of community supply of antiviral and antibacterial agents from community pharmacies during the COVID-19 pandemic in selected countries in eastern Europe and central Asia. Where there was no suitable electronic system for collecting and analysing data on medicine purchases, prescriptions and use, manual data-collection methods were used to capture this information. In Serbia, the health information system collects data on medicines dispensed and reimbursed under the national health insurance programme. This electronic system allowed extraction of relevant data on antimicrobials dispensed and was used in the study.

2. THE STUDY

2.1 Study objective

The objective of the study was to assess the patterns of consumption of antimicrobials sourced from community pharmacies during the COVID-19 pandemic.

2.2 Methods

Nine countries – Armenia, Georgia, Kazakhstan, Kyrgyzstan, North Macedonia, the Russian Federation, Serbia, Tajikistan and Uzbekistan – participated in this cross-sectional study. In all but Serbia, the study involved data collection from a random sample of community pharmacies from the capital city and several regions within each participating country.

A minimum of 25 pharmacies in the capital city and 10 in each of the participating regions was sought to enable comparisons of patterns of supply between urban and rural settings.

Where possible, pharmacies were randomly selected for inclusion in the study. Informed consent was obtained from participating pharmacies, which were then allocated a code number known only to the investigators managing the study at country level. Only the study number (pharmacy number) was recorded on the data-collection form.

Pharmacists from participating pharmacies were asked to record all episodes of supply of antimicrobial agents to customers during a one-week period. A minimum of 25 encounters was sought from each participating pharmacy. Information was recorded on the date of supply, the age and gender of the patient/client and the antimicrobials sold, including the name and the type of formulation (oral, injectable). Pharmacists were also asked to record whether the request/supply was based on presentation of a prescription or not.

Pharmacists were asked to note the reason for the supply, such as presenting symptoms or a presumptive or confirmed diagnosis. This allowed examination of supplies related to COVID-19 infection and other common infections. Where possible, medicines supplied for URTIs and urinary tract infections (UTIs) were compared with WHO-recommended treatment choices *(2)*.

Data were sought from a minimum of 1000 encounters in which an antimicrobial was supplied in each participating country. Data were aggregated and presented at regional and national levels, not at individual pharmacy level.

A draft of the WHO-approved data-collection form used in the study is shown in Annex 1. In some cases, local data-collection forms were modified in accordance with local information needs and following approval from local ethics committees.

At country level, a study coordinator was appointed for each capital city and regional area included in the study to oversee data collection. The study coordinator was responsible for data entry for all participating pharmacies in regions.

Dates of data collection varied between participating countries. Differences in timing related to obtaining local ethics committee approvals (where required) and recruiting study coordinators and participating pharmacists. Data collection for all eight studies occurred between August 2020 and March 2021, which was, in each case, during the first year of the ongoing COVID-19 pandemic.

The epidemiological context varied between countries, but in all countries the studies were conducted well after WHO declared the outbreak of a Public Health Emergency of International Concern (30 January 2020) and a pandemic (11 March 2020). On 24 January 2020, Bordeaux, France, was the first city in the European Region to report a case of COVID-19. From 27 February 2020, Romania's 24/7 national hotline, Tel Verde [Green Line], responded to calls from Romanians asking for the latest information and advice on COVID-19. Overall, countries in eastern Europe experienced lower caseloads of COVID-19 patients in the first half of 2020 compared to western Europe, with a major surge of cases and deaths towards the end of 2020.

In Serbia, data were extracted from the health information system that collects data on dispensed medicines in all public and 90% of private community pharmacies. Data were obtained on supply of antimicrobials for the week of 13–19 April 2020. Given the availability of data from the reimbursement system, patterns of supply of antimicrobials were compared with the same week in 2019 to examine changes in volume and choices of agents prescribed that might be attributable in part to COVID-19 infection.

2.3 Ethics approval

The master protocol for the study was developed by the Access to Medicines and Health Products team at the WHO Regional Office for Europe and approved by the WHO Human Research Ethics Committee (WHO HREC, approval number 0003376). The master protocol was modified for use at country level. Each national protocol was reviewed by the WHO HREC and national ethics committee where needed. In some countries, the WHO-approved protocol was deemed to provide sufficient ethical oversight and further national ethical review was not required.

2.4 Funding

The study was funded by the Ministry of Health, Welfare and Sport of the Netherlands and the German Collaboration Programme. Financial support was provided to each participating country to cover costs for study coordinators, data collection by pharmacists, reimbursement for travel and other costs associated with data analysis and report writing.

2.5 National research teams

National research teams were established to coordinate each country study. The national teams could come from a university department, a professional pharmaceutical organization or a nominated agency within the ministry of health.

The data generated in this project remain the property of the national research teams.

3. RESULTS

Results from the studies conducted using manual data-collection methods (eight countries, Table 1) are reported in this chapter. The results for Serbia are described in Chapter 4.

Most of the eight national research teams were led by the national focal points of the WHO Europe Antimicrobial Medicines Consumption network in collaboration with other institutions.

All eight studies included pharmacies in the capital city and between four and seven regions of the country.

The results of the regional analyses are beyond the scope of this crossnational report. Additional analyses conducted at regional level are provided in country-level reports.

Table 1. Study sites

Country	Research sites	
	Capital city	Number of regions outside the capital city
Armenia	Yerevan	5
Georgia	Tbilisi	6
Kazakhstan	Nur-Sultan	6
Kyrgyzstan	Bishkek	7
North Macedonia	Skopje	4
Russian Federation	Moscow	4
Tajikistan	Dushanbe	5
Uzbekistan	Tashkent	4

3.1 Description of pharmacies and encounters

Across the eight countries, 622 pharmacies participated in the study, ranging from 56 in North Macedonia to 96 in Kyrgyzstan (Table 2).

Most of the participating pharmacies in all eight countries were in the private sector and generally were a mix of chain or network pharmacies and private independent pharmacies. Only the Russian Federation and Uzbekistan included public pharmacies in their studies.

Table 2. Numbers of participating pharmacies and encounters

Country	Total number of pharmacies	Sector			Urban (%)	Rural (%)	Number of encounters recorded nationally
		Public pharmacy	Private chain pharmacy	Private independent pharmacy			
Armenia	75	0	34	41	74 (98.7%)	1 (1.3%)	**1 953**
Georgia	75	0	50	25	67 (89.3%)	8 (10.7%)	**1 656**
Kazakhstan	82	0	80	2	82 (100.0%)	0 (0.0%)	**1 937**
Kyrgyzstan	96	0	61	35	36 (37.5%)	60 (62.5%)	**1 220**
North Macedonia	56	0	35	21	53 (94.6%)	3 (5.4%)	**2 136**
Russian Federation	71	30	37	4	70 (98.6%)	1 (1.4%)	**5 270**
Tajikistan	75	0	56	19	46 (61.3%)	29 (38.7%)	**1 853**
Uzbekistan	92	54	38[a]	–	60 (65.2%)	32 (34.8%)	**9 818**
Total	**622**	**84**	**–**	**–**	**488**	**134**	**25 843**

[a] Private only. No information available on chain or independent

Most pharmacies in each country were in an urban location. Kyrgyzstan, Tajikistan and Uzbekistan were notable exceptions, with 62.5%, 38.7% and 34.8% of participating pharmacies defined as being in a rural location. Across most country studies there were insufficient numbers of rural pharmacies included for meaningful urban/rural comparisons.

Information was available for 25 843 community pharmacy encounters in which one or more antimicrobials were supplied during the week of data collection, ranging from 1220 encounters in 96 pharmacies in Kyrgyzstan to 9818 encounters in 92 pharmacies in Uzbekistan.

3.2 Gender and age distribution

All countries except Tajikistan and Uzbekistan recorded more encounters with females than males, ranging from 60.2% of encounters in the Russian Federation to 53% in North Macedonia (Table 3). Encounters with females represented 48.2% and 42.1% of encounters in Tajikistan and Uzbekistan.

Table 3. Gender distribution of encounters

Country	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan
Number of encounters	1 953	1 656	1 937	1 220	2 136	5 270	1 853	9 818
Female, n (%)	1 097 (56.2%)	887 (53.6%)	1 043 (53.8%)	695 (56.9%)	1 133 (53.0%)	3 173 (60.2%)	893 (48.2%)	4 132 (42.1%)
Male, n (%)	856 (43.8%)	769 (46.4%)	894 (46.2%)	526 (43.1%)	988 (46.3%)	2 097 (39.8%)	960 (51.8%)	5 647 (57.5%)

The age distribution of customers included in the studies is shown in Table 4. In all eight country studies, most customers were aged 19–60 years. The proportion of encounters in those aged 19–35 years ranged from 18.2% in North Macedonia to 46.8% in Uzbekistan. Encounters in those aged 36–60 years ranged from 39.5% in Kazakhstan to 52.2% in Armenia.

Relatively few encounters were recorded for customers aged 12 years or younger – fewer than 10% in all countries except in Kyrgyzstan. Reported encounters for customers aged over 60 years ranged from 2.7% in Kyrgyzstan to 26.1% in North Macedonia.

Table 4. Age distribution of encounters

Country	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan
Total number of encounters	1 953	1 656	1 937	1 220	2 136	5 270	1 853	9 818
< 5 years, n (%)	25 (1.3%)	31 (1.9%)	56 (2.9%)	76 (6.2%)	51 (2.4%)	57 (1.1%)	10 (0.5%)	11 (0.1%)
5–12 years, n (%)	53 (2.7%)	115 (6.9%)	101 (5.2%)	97 (8.0%)	84 (3.9%)	90 (1.7%)	35 (1.9%)	373 (3.8%)
13–18 years, n (%)	23 (1.2%)	77 (4.6%)	60 (3.1%)	38 (3.1%)	67 (3.1%)	67 (1.3%)	92 (5.0%)	400 (4.1%)
19–35 years, n (%)	617 (31.6%)	485 (29.3%)	831 (42.9%)	470 (38.5%)	388 (18.2%)	1 503 (28.5%)	801 (43.2%)	4 590 (46.8%)
36–60 years, n (%)	1 019 (52.2%)	675 (40.8%)	765 (39.5%)	506 (41.5%)	911 (42.6%)	2 610 (49.5%)	820 (44.3%)	4 118 (41.9%)
> 60 years, n (%)	216 (11.1%)	273 (16.5%)	122 (6.3%)	33 (2.7%)	558 (26.1%)	943 (17.9%)	95 (5.1%)	316 (3.2%)

3.3 Description of encounters

The number of encounters included in the country studies varied from 1220 (Kyrgyzstan) to 9818 (Uzbekistan). Between 1240 antimicrobials (Kyrgyzstan) and 9967 (Uzbekistan) were supplied during the encounters (Table 5).

Table 5. Description of encounters

Country	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan
Number of encounters	1 953	1 656	1 937	1 220	2 136	5 270	1 853	9 818
Number of antimicrobials supplied	2 360	1 685	1 952	1 240	2 239	5 514	2 876	9 967
Average number of antimicrobials per encounter	1.20	1.02	1.01	1.02	1.05	1.05	1.55	1.02
Encounters with more than one antimicrobial supplied, n (%)	354 (18.1%)	30 (1.8%)	16 (0.8%)	21 (1.7%)	87 (4.1%)	220 (4.2%)	821 (44.3%)	140 (1.4%)
Encounters with supply of oral and parenteral antimicrobials, n (%)	78 (4.0%)	12 (0.7%)	5 (0.3%)	3 (0.2%)	0 (0.0%)	21 (0.4%)	537 (29%)	55 (0.6%)

Table 5 contd

Country	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan
Average days of supply of antimicrobial in days								
Oral	NA	5.3	5.7	NA	6.4	NA	4.8	NA
Parenteral	NA	5.8	6.6	NA	5.3	NA	5.9	NA
Reason for use recorded, n (%)	2 360 (100.0%)	1 685 (100.0%)	1 947 (99.7%)	1 240 (100.0%)	2 201 (98.3%)	5 511 (99.9%)	2 875 (100.0%)	9 950 (99.8%)
Source of request recorded								
Prescription, n (%)	1 131 (47.9%)	1 496 (88.8%)	1 708 (87.8%)	923 (74.4%)	2 165 (97.1%)	3 889 (70.5%)	629 (22.7%)	4 483 (45.0%)
Emergency supply, n (%)	0 (0.0%)	0 (0.0%)	130 (6.7%)	0 (0.0%)	65 (2.9%)	58 (1.1%)	186 (6.7%)	2 625 (26.3%)
Other, n (%)	1 229 (52.1%)	189 (11.2%)	108 (5.5%)	317 (25.6%)	0 (0.0%)	1 567 (28.4%)	1 961 (70.6%)	2 859 (28.7%)

NA: not available.

There was little variation in the average number of antimicrobials supplied per encounter – from 1.01 antimicrobials per encounter in Kazakhstan to 1.55 in Tajikistan.

The percentage of encounters across the country studies resulting in supply of more than one antimicrobial ranged from 0.8% in Kazakhstan to 44.3% in Tajikistan. The proportion of encounters where clients were supplied with both an oral and an injectable antimicrobial ranged from 0% in North Macedonia to 29% in Tajikistan.

Information on the average number of days of supply for oral antimicrobials was not available in all studies. Where this information was available, average days of supply ranged from 4.8 in Tajikistan to 6.4 in North Macedonia. For parenteral formulations, the average duration of supply ranged from 5.3 days (North Macedonia) to 6.6 days (Kazakhstan).

Pharmacists recorded a "reason for use" in almost all encounters included in the country studies.

The proportion of encounters related to presentation of a prescription ranged from 22.7% of encounters in Tajikistan to 97.1% in North Macedonia. Only Uzbekistan reported a significant number of supplies under the category "emergency supply". More than half the encounters in Armenia (52.1%) and Tajikistan (70.6%) were reported as "other" and no further information on this category is available.

3.4 Antimicrobial formulations supplied

Supplies of oral and parenteral formulations varied across the country studies (Table 6). Across all Anatomical Therapeutic Chemical (ATC) categories, oral formulations were the most commonly supplied medicine type, ranging from 56.3% of encounters in Tajikistan to 99.2% in North Macedonia.

Reasons for higher numbers of supplies of parenteral formulations in community pharmacies in Kazakhstan (24.5% of encounters), Kyrgyzstan (31.9%) and Tajikistan (43.7%) are worthy of further investigation to determine if supplies reflect cultural, age or prescriber preferences.

Across all encounters, ATC code J01 antimicrobial agents were most often supplied, representing between 61.9% (the Russian Federation) and 96% (North Macedonia) of all antimicrobials supplied where information on formulation type was recorded.

Only one country study reported significant numbers of supplies of ATC code J05 antivirals for systemic use – the Russian Federation, with 1194 supplies of J05 antivirals (26.7% of supplies where formulation type was reported) (Table 6).

Table 6. Formulation type supplied

Country	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan
Number of encounters	1 953	1 656	1 937	1 220	2 136	5 270	1 853	9 818
Number of antimicrobials supplied	2 360	1 685	1 952	1 240	2 239	5 514	2 876	9 967
Information on formulation (oral/ parenteral), all ATC codes	**2 208**	**1 591**	**1 782**	**1 208**	**2 094**	**4 467**	**2 764**	**8 591**
Oral, n (%)	1 998 (90.5%)	1 297 (81.5%)	1 346 (75.5%)	815 (68.1%)	2 078 (99.2%)	4 233 (94.8%)	1 555 (56.3%)	6 701 (78.0%)
Parenteral, n (%)	210 (9.5%)	294 (18.5%)	436 (24.5%)	382 (31.9%)	16 (0.8%)	234 (5.2%)	1 209 (43.7%)	1 890 (22.0%)
J01 antimicrobials supplied	**1 646**	**1 438**	**1 410**	**901**	**2 011**	**2 736**	**1 734**	**7 393**
Oral, n (%)	1 438 (87.4%)	1 144 (79.6%)	976 (69.2%)	557 (61.8%)	1 995 (99.2%)	2 521 (92.1%)	663 (38.2%)	5 616 (76.0%)
Parenteral, n (%)	208 (12.6%)	294 (20.4%)	434 (30.8%)	344 (38.2%)	16 (0.8%)	215 (7.9%)	1 071 (61.8%)	1 777 (24.0%)
J05 antimicrobials supplied	**90**	**16**	**162**	**77**	**12**	**1 194**	**217**	**15**
Oral, n (%)	88 (97.8%)	16 (100%)	162 (100%)	76 (98.7%)	12 (100%)	1 194 (100%)	217 (100%)	15 (100%)
Parenteral, n (%)	2 (2.2%)	0 (0.0%)	0 (0.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
P01 antimicrobials supplied	**40**	**29**	**42**	**38**	**10**	**97**	**180**	**675**
Oral, n (%)	40 (100.0%)	29 (100.0%)	42 (100.0%)	33 (86.8%)	10 (100.0%)	97 (100.0%)	78 (43.3%)	675 (100.0%)
Parenteral, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (13.2%)	0 (0.0%)	0 (0.0%)	102 (56.7%)	0 (0.0%)

Given the relatively smaller numbers of supplies of ATC J05 and P01 antimicrobials, subsequent analyses focus on the J01 group of antibacterials.

3.4.1 J01 antibacterials supplied by gender and age

There was no evidence in the country studies to suggest differences in formulations of J01 antibacterials supplied to female and male customers (Table 7). Notably, in the three countries with the highest rates of supply of parenteral formulations (Kazakhstan, Kyrgyzstan and Tajikistan), rates of supply of parenteral formulations were similar for females and males.

Table 7. Formulation type by gender (J01 antimicrobials)

Country	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan
Number of J01 antimicrobials supplied	**1 646**	**1 438**	**1 410**	**901**	**2 011**	**2 736**	**1 734**	**7 393**
Oral, n (%)	1 438 (87.4%)	1 144 (79.6%)	976 (69.2%)	557 (61.8%)	1 995 (99.2%)	2 521 (92.1%)	663 (38.2%)	5 616 (76.0%)
Parenteral, n (%)	208 (12.6%)	294 (20.4%)	434 (30.8%)	344 (38.2%)	16 (0.8%)	215 (7.9%)	1 071 (61.8%)	1 777 (24.0%)
Female	**906**	**738**	**705**	**511**	**1 062**	**1 563**	**800**	**2 851**
Oral, n (%)	794 (87.6%)	602 (81.6%)	504 (71.5%)	311 (60.9%)	1 056 (99.4%)	1 432 (91.6%)	294 (36.8%)	2 110 (74.0%)
Parenteral, n (%)	112 (12.4%)	136 (18.4%)	201 (28.5%)	200 (39.1%)	6 (0.6%)	131 (8.4%)	506 (63.3%)	741 (26.0%)
Male	**740**	**700**	**705**	**390**	**940**	**1 173**	**934**	**4 540**
Oral, n (%)	644 (87.0%)	542 (77.4%)	472 (67.0%)	246 (63.1%)	931 (99.0%)	1 089 (92.8%)	369 (39.5%)	3 504 (77.2%)
Parenteral, n (%)	96 (13.0%)	158 (22.6%)	233 (33.0%)	144 (36.9%)	9 (1.0%)	84 (7.2%)	565 (60.5%)	1 036 (22.8%)

There was some evidence to suggest differences in formulations of J01 antibacterials supplied according to age (Table 8). In general, supplies of parenteral formulations to younger customers were low, with highest rates of supply to customers aged over 60 years. Country differences were noted, however. In Georgia, for example, parenteral formulations represented 20.4% of J01 supplies. Rates of supply of parenteral formulations were 0% for those aged less than 12 years, 5.3% for those aged 13–18 years, 15.6% for those aged 19–35 years, 28.1% for those aged 36–60 years and 28.5% of supplies were for those aged over 60 years. In Tajikistan, however, where parenteral forms represented 61.8% of J01 supplies, rates of supply were relatively high across all age groups. Rates were 75% for those aged less than 5 years (although based on small numbers), 43.3% for 5–12-year-olds, 52.3% for 13–18 years, 58.6% for 19–35 years, 65.9% for 36–60 years and 65.2% of supplies were for those aged over 60 years.

Table 8. Formulation type supplied by age group (J01 antimicrobials)

Country	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan
Number of J01 antimicrobials supplied	**1 646**	**1 438**	**1 410**	**901**	**2 011**	**2 736**	**1 734**	**7 393**
Oral, n (%)	1 438 (87.4%)	1 144 (79.6%)	976 (69.2%)	557 (61.8%)	1 995 (99.2%)	2 521 (92.1%)	663 (38.2%)	5 616 (76.0%)
Parenteral, n (%)	208 (12.6%)	294 (20.4%)	434 (30.8%)	344 (38.2%)	16 (0.8%)	215 (7.9%)	1 071 (61.8%)	1 777 (24.0%)
< 5 years	**24**	**30**	**51**	**58**	**48**	**44**	**8**	**11**
Oral, n (%)	22 (91.7%)	30 (100.0%)	50 (98.0%)	36 (62.1%)	48 (100.0%)	44 (100.0%)	2 (25.0%)	11 (100.0%)
Parenteral, n (%)	2 (8.3%)	0 (0.0%)	1 (2.0%)	22 (37.9%)	0 (0.0%)	0 (0.0%)	6 (75.0%)	0 (0.0%)
5–12 years	**50**	**114**	**87**	**69**	**80**	**67**	**30**	**358**
Oral, n (%)	49 (98.0%)	114 (100.0%)	67 (77.0%)	46 (66.7%)	79 (98.8%)	67 (100.0%)	17 (56.7%)	322 (89.9%)
Parenteral, n (%)	1 (2.0%)	0 (0.0%)	20 (23.0%)	23 (33.3%)	1 (1.3%)	0 (0.0%)	13 (43.3%)	36 (10.1%)

Table 8 contd

Country	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan
13–18 years	**20**	**76**	**37**	**29**	**58**	**37**	**88**	**284**
Oral, n (%)	18 (90.0%)	72 (94.7%)	31 (83.8%)	19 (65.5%)	58 (100.0%)	35 (94.6%)	42 (47.7%)	239 (84.2%)
Parenteral, n (%)	2 (10.0%)	4 (5.3%)	6 (16.2%)	10 (34.5%)	0 (0.0%)	2 (5.4%)	46 (52.3%)	45 (15.8%)
19–35 years	**508**	**424**	**565**	**327**	**355**	**690**	**730**	**3 349**
Oral, n (%)	475 (93.5%)	358 (84.4%)	391 (69.2%)	219 (67.0%)	348 (98.0%)	649 (94.1%)	302 (41.4%)	2 418 (72.2%)
Parenteral, n (%)	33 (6.5%)	66 (15.6%)	174 (30.8%)	108 (33.0%)	7 (2.0%)	41 (5.9%)	428 (58.6%)	931 (27.8%)
36–60 years	**858**	**545**	**571**	**392**	**871**	**1 448**	**786**	**3 268**
Oral, n (%)	729 (85.0%)	392 (71.9%)	381 (66.7%)	225 (57.4%)	868 (99.7%)	1 335 (92.2%)	268 (34.1%)	2 585 (79.1%)
Parenteral, n (%)	129 (15.0%)	153 (28.1%)	190 (33.3%)	167 (42.6%)	3 (0.3%)	113 (7.8%)	518 (65.9%)	683 (20.9%)
> 60 years	**186**	**249**	**98**	**26**	**546**	**450**	**92**	**114**
Oral, n (%)	145 (78.0%)	178 (71.5%)	55 (56.1%)	12 (46.2%)	543 (99.3%)	391 (86.9%)	32 (34.8%)	38 (33.3%)
Parenteral, n (%)	41 (22.0%)	71 (28.5%)	43 (43.9%)	14 (53.8%)	3 (0.7%)	59 (13.1%)	60 (65.2%)	76 (66.7%)

3.5 Choice of antimicrobials supplied by indication for treatment

Pharmacists were asked to record an indication for treatment for each antimicrobial supplied. This information was noted in 9937 cases.

URTI was the most recorded indication for treatment in each of the eight country studies and ranged from 32.8% of cases in Uzbekistan to 64.5% of cases in Georgia (Table 9). Instances of UTI ranged from 8.6% of encounters in Armenia to 25.7% in Georgia. COVID-19-related reasons for supply ranged from 0.5% in Georgia to 15.3% in Armenia. Recording of other not specified indications ranged from 0% in Georgia to 27.6% in Armenia.

Table 9. Recorded indications for treatment

Indication	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan
	Number of encounters (% of country total)							
URTI, n (%)	783 (33.2%)	1 086 (64.5%)	755 (38.8%)	502 (40.5%)	1 206 (54.8%)	2 028 (36.8%)	1 109 (38.6%)	3 263 (32.8%)
UTI, n (%)	202 (8.6%)	433 (25.7%)	367 (18.8%)	249 (20.1%)	193 (8.8%)	478 (8.7%)	626 (21.8%)	1 016 (10.2%)
Gastrointestinal infection, n (%)	95 (4.0%)	71 (4.2%)	75 (3.9%)	110 (8.9%)	55 (2.5%)	282 (5.1%)	269 (9.4%)	1 062 (10.7%)
Skin infection, n (%)	67 (2.8%)	34 (2.0%)	165 (8.5%)	74 (6.0%)	109 (5.0%)	666 (12.1%)	64 (2.2%)	758 (7.6%)
Eye infection, n (%)	3 (0.1%)	2 (0.1%)	73 (3.7%)	39 (3.1%)	49 (2.2%)	222 (4.0%)	50 (1.7%)	180 (1.8%)
Flu/influenza, n (%)	45 (1.9%)	5 (0.3%)	120 (6.2%)	139 (11.2%)	40 (1.8%)	455 (8.3%)	352 (12.2%)	1 074 (10.8%)
COVID-19, n (%)	361 (15.3%)	8 (0.5%)	20 (1.0%)	28 (2.3%)	279 (12.7%)	462 (8.4%)	205 (7.1%)	701 (7.1%)

Table 9 contd

Indication	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan
	Number of encounters (% of country total)							
Hospital treatment related, n (%)	152 (6.4%)	46 (2.7%)	46 (2.4%)	32 (2.6%)	6 (0.3%)	28 (0.5%)	25 (0.9%)	1 229 (12.4%)
"Other indications", n (%)	652 (27.6%)	0 (0.0%)	326 (16.7%)	67 (5.4%)	265 (12.0%)	890 (16.1%)	175 (6.1%)	654 (6.6%)
Total encounters	**2 360**	**1 685**	**1 947**	**1 240**	**2 202**	**5 511**	**2 875**	**9 937**

3.5.1 Top 10 antimicrobials supplied for treatment of URTI

Table 10 shows the most supplied antibacterial agents supplied for encounters recorded as URTI and includes countries where the agent was in the top 10 most supplied agent in at least two of the eight participating countries. Notable is the large number of different agents supplied, with 14 oral and 18 parenteral agents included in the top 10 in at least two of the country studies.

The most often supplied oral agents nevertheless were broadly consistent across countries. Azithromycin was the most frequently supplied agent in five of the eight countries and was ranked second in a further three. Only one other oral medicine, amoxicillin, was included in the top 10 agents for URTI in all eight countries. The fluoroquinolones ciprofloxacin and levofloxacin were included in the top 10 agents in six and seven countries respectively.

Most of the supplied oral agents were from the ATC J01 group. One antifungal agent, fluconazole (J02AC01), was reported in the top 10 oral agents for URTI in two countries. The antiviral agent umifenovir (J05AQX13) was included in the top 10 agents for URTI in three countries.

All top 10 parenteral agents reported were from the ATC J01 group. The cephalosporin ceftriaxone was ranked first in seven countries and second in the remaining country. A second cephalosporin, cefotaxime, was included in the top 10 parenteral agents in six countries.

Table 10. Country rankings of top 10 antimicrobials supplied for treatment of URTI

Oral										
ATC	**Agent**	**Armenia**	**Georgia**	**Kazakhstan**	**Kyrgyzstan**	**North Macedonia**	**Russian Federation**	**Tajikistan**	**Uzbekistan**	**Number of countries[a]**
J01FA10	Azithromycin	1	1	1	2	1	2	2	1	8
J01CA04	Amoxicillin	3	3	2	1	4	3	3	5	8
J01MA12	Levofloxacin	5	4	5	5	–	6	4	2	7
J01CR02	Amoxicillin + beta-lactamase inhibitor	2	2	3	3	2	1	10	–	7
J01MA02	Ciprofloxacin	6	–	4	4	6	8	–	3	6
J01FA09	Clarithromycin	–	8	9	7	7	–	–	6	5
J01DD08	Cefixime	7	5	10	–	3	5	–	–	5
J01EE01	Sulfamethoxazole + trimethoprim	4	–	10	6	–	–	6	–	4
J01CA01	Ampicillin	–	7	7	–	–	–	–	4	3

Table 10 contd

Oral										
ATC	**Agent**	**Armenia**	**Georgia**	**Kazakhstan**	**Kyrgyzstan**	**North Macedonia**	**Russian Federation**	**Tajikistan**	**Uzbekistan**	**Number of countries[a]**
J05AX13	Umifenovir	–	–	7	–	–	7	5	–	3
J01DC02	Cefuroxime	–	–	6	–	5	–	–	–	2
J01FA03	Midecamycin	9	–	–	–	10	–	–	–	2
J01DB01	Cefalexin	10	–	–	–	8	–	–	–	2
J02AC01	Fluconazole	–	–	–	7	–	–	1	–	2
Parenteral										
ATC	**Agent**	**Armenia**	**Georgia**	**Kazakhstan**	**Kyrgyzstan**	**North Macedonia**	**Russian Federation**	**Tajikistan**	**Uzbekistan**	**Number of countries[a]**
J01DD04	Ceftriaxone	1	1	1	1	2	1	1	1	8
J01DD01	Cefotaxime	2	10	7	–	–	3	8	7	6
J01DB04	Cefazolin	3	–	2	–	–	4	5	2	5
J01CA01	Ampicillin	3	–	7	3	–	–	2	5	5
J01MA12	Levofloxacin	–	–	4	2	–	7	3	10	5
J01GB03	Gentamicin	–	3	7	9	1	–	–	–	4
J01CR01	Ampicillin + beta-lactamase inhibitor	3	2	–	6	–	–	7	–	4
J01DD02	Ceftazidime	–	7	5	–	–	–	8	8	4
J01FF02	Lincomycin	–	9	–	–	2	4	–	–	3
J01DC02	Cefuroxime	3	–	3	–	–	–	–	–	2
J01GB06	Amikacin	–	4	–	–	–	–	–	9	2
J01CE01	Benzylpenicillin	–	7	7	–	–	–	–	–	2
J01XD01	Metronidazole	–	–	5	–	–	7	–	–	2
J01DE01	Cefepime	–	–	–	7	–	–	6	–	2
J01DD62	Cefoperazone + beta-lactamase inhibitor	–	5	–	–	–	–	–	5	2
J01DD63	Ceftriaxone + beta-lactamase inhibitor	–	6	–	9	–	–	–	–	2
J01GA01	Streptomycin	–	10	–	–	–	–	–	4	2
J01CR02	Amoxicillin + beta-lactamase inhibitor	–	–	–	5	–	7	–	–	2

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Rankings are reported for agents that were included in the top 10 in two or more countries. This means that in some cases, rankings will be missing because an antibiotic is in the top 10 of only one country.

[a] Number of countries that have this agent in their top 10.

3.5.2 Top 10 antimicrobials supplied for treatment of COVID-19

COVID-19-related reasons for antimicrobial supply (2064 encounters) ranged from 0.5% of encounters in Georgia to 15.3% in Armenia (Table 9). Agents supplied for this indication (top 10 rankings) are shown in Table 11. Notable is the large number of different agents supplied, with 13 oral agents and eight parenteral included in the top 10 agents across the country studies.

The quinolone levofloxacin was the only oral agent included in the top 10 in all eight countries; it was ranked first in two countries. Azithromycin was the first-ranked agent in five countries but was not included in the top 10 in Georgia. Early in the pandemic, azithromycin was proposed as a treatment for COVID-19, with in vitro studies suggesting activity against some viruses, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) *(3,4)*.

Two antiviral agents were included in the top 10 – umifenovir (J05AX13, included in the top 10 for five countries) and oseltamivir (J05AH02, two countries). Umifenovir was ranked as the most supplied oral agent in Kyrgyzstan, while oseltamivir was ranked first in Kazakhstan.

Several other antiviral agents were included in the top 10 agents for just one country – rimantadine (J05CA02, Kyrgyzstan, rank 4), inosine pranobex (J05AX05, Kyrgyzstan, equal rank 4), imidazolyl ethanamide pentadioic acid (J05AX21, Russian Federation, rank 5), favipiravir (J05AX27, Russian Federation, rank 6), tilorone (J05AX19, Armenia, rank 7) and aciclovir (J05AB01, Armenia, equal rank 7).

Hydroxychloroquine (P01BA02) was ranked second for supply in Georgia and Uzbekistan. Like azithromycin, hydroxychloroquine was suggested early in the pandemic as a possible prevention method or treatment for COVID-19, given evidence of in vitro inhibition of SARS-CoV-2 *(5)*.

A range of parenteral agents was reported as being supplied for the treatment of COVID-19 infection. Ceftriaxone and levofloxacin were most widely used, with each included in the top 10 parenteral agents in six countries.

Table 11. Country rankings of top 10 antimicrobials supplied for treatment of COVID-19 infection

Oral										
ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
J01MA12	Levofloxacin	2	1	3	1	9	3	4	3	8
J01FA10	Azithromycin	1	–	3	1	1	1	2	1	7
J05AX13	Umifenovir	5	–	3	1	–	2	3	–	5
J01CA04	Amoxicillin	10	–	3	–	7	7	–	–	4
J01MA02	Ciprofloxacin	7	–	–	–	5	–	–	5	3
J01CR02	Amoxicillin + beta-lactamase inhibitor	6	–	3	–	–	4	–	–	3
J01EE01	Sulfamethoxazole + trimethoprim	10	–	–	4	–	–	8	–	3
P01BA02	Hydroxychloroquine	–	2	–	–	–	9	–	2	3
J01FA09	Clarithromycin	–	–	3	–	6	10	–	–	3
J01DD08	Cefixime	4	–	–	–	2	–	–	–	2
J02AC01	Fluconazole	–	–	–	–	–	–	1	3	2
J01MA14	Moxifloxacin	3	–	–	–	3	–	–	–	2
J05AH02	Oseltamivir	–	–	1	–	–	8	–	–	2

Table 11 contd

Parenteral										
ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
J01DD04	Ceftriaxone	1	–	2	–	1	1	4	4	6
J01MA12	Levofloxacin	3	–	1	1	–	3	1	2	6
J01DH02	Meropenem	–	–	4	2	–	–	3	4	4
J01MA02	Ciprofloxacin	4	–	–	2	–	–	8	–	3
J01MA14	Moxifloxacin	2	–	–	2	–	–	–	–	2
J01DE01	Cefepime	–	–	–	2	–	–	5	–	2
J01DD01	Cefotaxime	–	–	–	–	–	2	8	–	2
J02AC01	Fluconazole	–	–	–	–	–	–	6	1	2

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Rankings are reported for agents that were included in the top 10 in two or more countries. This means that in some cases, rankings will be missing because an antibiotic is in the top 10 of only one country.

[a] Number of countries that have this agent in their top 10.

3.5.3 Top 10 antimicrobials supplied for treatments associated with hospital care

In total, 1564 cases of supply of antimicrobials were linked to hospital care (Table 9). The medicines supplied are shown in Table 12.

Ten oral and 18 parenteral agents were included in this top 10 analysis. Seven of the oral agents were from ATC class J01, one was an antifungal agent (fluconazole (J02AC01), included in the top 10 for five countries), one was an agent with antibacterial and antiprotozoal actions (metronidazole (P01AB01), four countries) and one an antiviral agent (umifenovir (J05AX13), two countries). Umifenovir was ranked as the most supplied oral agent in the Russian Federation.

All the parenteral agents reported in the top 10 analysis were from the J01 category. Ceftriaxone was the most often supplied parenteral agent, being included in the top 10 for seven countries, in which it was ranked first to third.

Table 12. Country rankings of top 10 antimicrobials supplied for treatments associated with hospital care

Oral										
ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
J02AC01	Fluconazole	1	1	–	7	–	–	1	10	5
J01CR02	Amoxicillin + beta-lactamase inhibitor	6	–	2	2	2	2	–	–	5
J01FA10	Azithromycin	2	–	–	1	–	–	2	4	4
J01MA12	Levofloxacin	4	1	–	2	–	–	–	2	4
P01AB01	Metronidazole	9	–	2	2	–	–	–	5	4
J01MA02	Ciprofloxacin	9	–	1	2	1	–	–	–	4

Table 12 contd

Oral										
ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
J01CA04	Amoxicillin	9	–	–	2	–	4	–	–	3
J05AX13	Umifenovir	6	–	–	–	–	1	–	–	2
J01DD08	Cefixime	9	–	–	–	–	4	–	–	2
J01MA14	Moxifloxacin	9	–	–	–	–	–	–	5	2
Parenteral										
ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
J01DD04	Ceftriaxone	1	3	1	–	2	2	2	2	7
J01XD01	Metronidazole	6	–	4	1	–	3	–	8	5
J01DD01	Cefotaxime	2	–	10	–	–	–	5	5	4
J01DH02	Meropenem	9	–	4	–	–	–	5	3	4
J01DE01	Cefepime	9	4	3	–	–	–	–	10	4
J01GB06	Amikacin	8	–	6	–	–	–	5	–	3
J01DB04	Cefazolin	6	–	10	–	–	–	–	1	3
J01MA12	Levofloxacin	9	–	–	–	–	–	2	6	3
J01DD62	Cefoperazone + beta-lactamase inhibitor	–	2	6	–	–	–	–	7	3
J01GB03	Gentamicin	–	–	10	–	–	–	5	4	3
J01MA02	Ciprofloxacin	4	–	–	–	1	–	–	–	2
J01MA01	Ofloxacin	–	–	10	–	–	–	5	–	2
J01MA14	Moxifloxacin	3	–	10	–	–	–	–	–	2
J01DC02	Cefuroxime	4	–	2	–	–	–	–	–	2
J01DD12	Cefoperazone	9	–	6	–	–	–	–	–	2
J01CR01	Ampicillin + beta-lactamase inhibitor	–	5	–	–	–	–	5	–	2
J01CE01	Benzylpenicillin	–	7	–	–	–	–	–	8	2
J01FF02	Lincomycin	–	–	10	–	–	1	–	–	2

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Rankings are reported for agents that were included in the top 10 in two or more countries. This means that in some cases, rankings will be missing because an antibiotic is in the top 10 of only one country.

[a] Number of countries that have this agent in their top 10.

3.5.4 Top 10 antimicrobials supplied for treatments associated with influenza/flu

There were 2230 cases of supply where influenza/flu was the reported reason for treatment (Table 9). The medicines supplied are shown in Table 13.

Among the 20 oral medicines, seven were antiviral agents and one was categorized as "other immunostimulants" (L03AX). The antiviral agents were inosine pranobex (J05AX05, included in the top 10 for five countries), umifenovir (J05AX13, five countries), aciclovir (J05AB01, five countries), tilorone (J05AX19, three countries), "other antivirals" (J05AX, three countries), rimantadine (J05AC02, two countries) and oseltamivir (J05AH02, two countries). Azithromycin (J01FA10) was the most supplied oral J01 agent and was included in the top 10 for six countries and ranked first in three.

All 11 parenteral agents in the top 10 were from the J01 category. The most often supplied was ceftriaxone, which was included in the top 10 for five countries and ranked first in four of these. The combination ceftriaxone + beta-lactamase inhibitor was included in the top 10 agents for two countries.

Table 13. Country rankings of top 10 antimicrobials supplied for treatments associated with influenza/flu

Oral										
ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
J01FA10	Azithromycin	–	–	4	3	1	6	1	1	6
J05AX05	Inosine pranobex	4	1	–	2	3	10	–	–	5
J05AX13	Umifenovir	1	–	3	6	–	1	2	–	5
J05AB01	Aciclovir	3	–	2	8	–	10	7	–	5
J01MA12	Levofloxacin	–	1	–	10	–	9	–	6	4
J01EE01	Sulfamethoxazole + trimethoprim	–	–	4	–	5	10	8	–	4
J01CA04	Amoxicillin	–	–	6	5	–	8	8	–	4
J01CR02	Amoxicillin + beta-lactamase inhibitor	–	–	9	6	4	7	–	–	4
J02AC01	Fluconazole	–	–	–	10	–	–	4	7	3
J05AX	Other antivirals	2	1	–	–	–	–	3	–	3
J05AX19	Tilorone	5	–	6	–	–	5	–	–	3
J01DD08	Cefixime	–	–	9	–	2	–	–	–	2
J01MA02	Ciprofloxacin	–	–	9	–	–	–	–	3	2
J01FA09	Clarithromycin	–	–	–	–	5	–	–	4	2
J01CA01	Ampicillin	–	–	–	–	–	10	–	2	2
J01DC02	Cefuroxime	–	–	6	–	5	–	–	–	2
J01MA14	Moxifloxacin	–	–	9	–	–	–	–	7	2
J05AC02	Rimantadine	–	–	–	4	–	2	–	–	2
J05AH02	Oseltamivir	–	–	1	–	–	4	–	–	2
L03AX	Other immunostimulants	–	–	–	1	–	–	6	–	2
Parenteral										
ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
J01DD04	Ceftriaxone	–	–	1	1	–	1	2	1	5
J01DB04	Cefazolin	–	–	2	3	–	–	–	2	3
J01MA12	Levofloxacin	–	–	–	3	–	–	4	3	3
J01CA01	Ampicillin	–	–	–	3	–	–	3	4	3
J01XD01	Metronidazole	–	–	2	–	–	–	8	–	2
J01DH02	Meropenem	–	–	2	–	–	–	–	8	2
J01GB03	Gentamicin	–	–	5	–	1	–	–	–	2
J01DD63	Ceftriaxone + beta-lactamase inhibitor	–	–	–	6	–	–	–	7	2
J01DD02	Ceftazidime	–	–	–	6	–	–	8	–	2
J01CR01	Ampicillin + beta-lactamase inhibitor	–	–	–	8	–	–	5	–	2
J01DE01	Cefepime	–	–	–	–	–	–	5	–	1

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Rankings are reported for agents that were included in the top 10 in two or more countries. This means that in some cases, rankings will be missing because an antibiotic is in the top 10 of only one country.

[a] Number of countries that have this agent in their top 10.

3.5.5 Top 10 antimicrobials supplied for treatment associated with UTI

There were 3564 occasions of supply where UTI was nominated as the reason for treatment (Table 9). The medicines supplied for treatment are shown in Table 14.

Eighteen oral and 15 parenteral agents were reported as being supplied for the treatment of UTI. Except for oral metronidazole (P01AB01) and fluconazole (J02AC01), all the agents were from the J01 class.

Oral forms of the fluoroquinolones ciprofloxacin and levofloxacin were included in the top 10 agents in all eight countries, with ciprofloxacin ranked first in five, second in one and third in one. Two other fluoroquinolones, norfloxacin and ofloxacin, were also included in five and two countries respectively.

Metronidazole and fluconazole were widely used and included in the top 10 agents in seven countries. The most widely supplied parenteral formulation for UTI was ceftriaxone.

Table 14. Country rankings of top 10 antimicrobials supplied for treatments associated with UTI

Oral										
ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
J01MA02	Ciprofloxacin	1	2	1	1	1	1	6	3	8
J01MA12	Levofloxacin	2	3	6	7	8	7	7	8	8
P01AB01	Metronidazole	6	7	3	3	–	9	9	2	7
J02AC01	Fluconazole	–	1	6	2	8	3	1	6	7
J01FA10	Azithromycin	10	–	6	6	6	–	3	4	6
J01MA06	Norfloxacin	2	–	4	5	2	5	–	–	5
J01AA02	Doxycycline	5	4	9	4	–	9	–	–	5
J01CR02	Amoxicillin + beta-lactamase inhibitor	6	–	–	7	4	4	–	–	4
J01DD08	Cefixime	4	10	–	–	2	9	–	–	4
J01XX07	Nitroxoline	–	–	–	9	–	–	5	1	3
J01XE03	Furazidin	–	4	–	–	–	6	9	–	3
J01DC02	Cefuroxime	10	–	9	–	5	–	–	–	3
J01EE01	Sulfamethoxazole + trimethoprim	–	–	5	–	7	–	4	–	3
J01FA09	Clarithromycin	9	–	–	–	8	–	–	5	3
J01XX01	Fosfomycin	–	6	2	–	–	2	–	–	3
J01MA01	Ofloxacin	–	–	–	–	–	–	9	7	2
J01CA04	Amoxicillin	–	–	–	9	–	–	7	–	2
J01XE01	Nitrofurantoin	6	–	–	–	–	7	–	–	2

Table 14 contd

Parenteral										
ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
J01DD04	Ceftriaxone	1	3	1	1	–	1	2	2	7
J01XD01	Metronidazole	3	–	2	2	–	–	1	1	5
J01MA02	Ciprofloxacin	3	–	5	3	–	–	4	–	4
J01DB04	Cefazolin	–	–	3	6	–	–	3	4	4
J01MA12	Levofloxacin	–	–	8	9	–	–	7	9	4
J01MA01	Ofloxacin	–	–	5	9	–	–	7	–	3
J01CA01	Ampicillin	–	–	–	4	–	–	5	7	3
J01DE01	Cefepime	3	–	–	9	–	–	9	–	3
J01GB06	Amikacin	–	1	–	–	–	–	9	9	3
J02AC01	Fluconazole	–	–	–	4	–	–	6	5	3
J01GB03	Gentamicin	–	–	8	–	–	–	–	7	2
J01DC02	Cefuroxime	2	–	8	–	–	–	–	–	2
J01MA14	Moxifloxacin	3	–	5	–	–	–	–	–	2
J01CR01	Ampicillin + beta-lactamase inhibitor	–	2	–	–	–	–	9	–	2
J01XX01	Fosfomycin	–	–	–	6	–	1	–	–	2

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Rankings are reported for agents that were included in the top 10 in two or more countries. This means that in some cases, rankings will be missing because an antibiotic is in the top 10 of only one country.

[a] Number of countries that have this agent in their top 10.

WHO guidance on the treatment of uncomplicated UTIs suggests that first-choice oral agents for lower UTI are nitrofurantoin, sulfamethoxazole + trimethoprim, trimethoprim, and amoxicillin + clavulanic acid *(6)*. These agents were included in the top 10 analyses in two, three, zero and four countries respectively. Nitroxoline (J01XX07) and furazidin (J01XE03) are closely related to nitrofurantoin and each of these agents was included in the top 10 for three countries.

WHO suggests first-choice treatment for mild-to-moderate pyelonephritis and prostatitis is ciprofloxacin, with ceftriaxone and cefotaxime as second-choice therapy *(7)*. It is recommended that severe pyelonephritis and prostatitis are treated with ceftriaxone or cefotaxime in addition to amikacin.

Fosfomycin parenteral, classified as a Reserve group antibiotic, was included in the top 10 parenteral agents for two countries. The WHO Access, Watch, Reserve (AWaRe) classification suggests that Reserve agents should be used for treatment of confirmed or suspected infections due to multidrug-resistant organisms and should be treated as "last resort" options *(8)*.

These observations suggest that opportunities exist to review national guidance on the management of UTIs to ensure recommendations align with best-practice international guidelines.

3.6 Antimicrobials supplied according to AWaRe classification

In April 2017, the Expert Committee on the Selection and Use of Essential Medicines proposed a categorization of antibiotics into Access, Watch and Reserve groups, with a fourth "unclassified"

category, with the classification to be revised as additional clinical syndromes are reviewed. The characteristics of these groups is as follows.

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, the use of which is neither evidence-based nor recommended in high-quality international guidelines. WHO does not recommend their use in clinical practice.

The AWaRe classification can be used to inform stewardship activities in community and hospital sectors by promoting greater use of Access agents, with lower resistance potential, and reduced consumption of Watch group antibiotics, which are at relatively higher risk of selection of bacterial resistance.

In 2019, WHO expanded the AWaRe classification to include 180 antibacterials used globally *(9)*. The revised AWaRe list encompasses medicines from the ATC group J01 and several additional agents: neomycin (ATC code A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), rifampicin (J04AB02), rifamycin (J04AB03), rifabutin (J04AB04) and metronidazole (P01AB01). In the absence of indication-linked information on antibiotic use, the WHO AWaRe classification allows a more detailed analysis of aggregated data and opportunities for stewardship activities *(10)*.

The full list of the top 20 oral and parenteral antibacterial agents included in the AWaRe classification and supplied across the eight studies are shown in Table A2.1 and Table A2.2 (see Annex 2). An abbreviated summary of the results is presented in Table 15 (oral agents) and Table 16 (parenteral agents). Table 15 shows the most supplied oral antibacterials and includes countries in which the agent was in the top 10 most supplied agents in at least two of the eight participating countries.

The Watch group agent azithromycin was ranked either as most supplied or second most supplied agent across all eight country studies. The Access group agents amoxicillin and amoxicillin + beta-lactamase inhibitor were generally ranked second to ninth in volumes of supply across the countries.

The number of supplies of the Watch group agents ciprofloxacin (country rankings one to five) and levofloxacin (rankings two to 14) was considerable. Rankings of levofloxacin illustrate some of the variability across countries – it was second most supplied agent in the Tajikistan study and fourteenth

most supplied in North Macedonia. Similarly, the Watch agent cefixime ranked second most supplied agent in the North Macedonia study but nineteenth in Tajikistan and fifteenth in Uzbekistan.

Only three agents were included in the top 10 for supplies in all eight country studies – amoxicillin (Access agent), azithromycin and ciprofloxacin (Watch group agents). Two agents – amoxicillin + beta-lactamase inhibitor (Access agent) and levofloxacin (Watch) – were reported in the top 10 agents for supply in seven of the eight country studies.

Table 15. Country rankings of top 20 oral antibacterials supplied

AWaRe	ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
Access	J01CA04	Amoxicillin	3	4	3	2	5	3	3	7	8
	P01AB01	Metronidazole	11	13	6	7	18	9	9	3	8
	J01AA02	Doxycycline	6	8	11	9	13	8	16	–	7
	J01CR02	Amoxicillin + beta-lactamase inhibitor	2	2	4	4	3	1	9	–	7
	J01EE01	Sulfamethoxazole + trimethoprim	8	–	10	8	17	13	4	20	7
Watch	J01DD08	Cefixime	7	6	12	13	2	6	19	15	8
	J01FA09	Clarithromycin	10	18	8	6	7	7	8	9	8
	J01FA10	Azithromycin	1	1	2	1	1	2	1	1	8
	J01MA02	Ciprofloxacin	5	5	1	3	4	5	5	2	8
	J01MA12	Levofloxacin	4	3	7	5	14	4	2	4	8
	J01DC02	Cefuroxime	13	–	5	–	6	14	–	–	4
	J01MA14	Moxifloxacin	8	16	–	–	10	–	–	18	4
	J01FA01	Erythromycin	–	9	–	10	–	–	6	–	3

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Agents included in the table are those antibacterials ranked in the top 10 in at least two participating countries. Rankings are reported for agents that were included in the top 10 in two or more countries. This means that in some cases, rankings will be missing because an antibiotic is in the top 10 of only one country. A full list of agents and rankings is shown in Annex 2, Tables A2.1 and A2.2. Agents included in this analysis are: antibacterials for systemic use (J01), neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), rifampicin (J04AB02), rifamycin (J04AB03), rifabutin (J04AB04) and metronidazole (P01AB01). The table is sorted according to the number of countries that included the antimicrobial in their top 20, considering Access (green) and Watch (yellow) agents separately *(9)*.

[a] Number of countries that have this agent in their top 20.

The Watch group agent ceftriaxone was ranked either most supplied or second most supplied parenteral agent across all eight country studies (Table 16). The Access group agents cefazolin and metronidazole were ranked in the top 10 agents supplied in six of the eight studies.

Beyond that, there was considerable crossnational variation in which parenteral antibacterials were supplied. For example, gentamicin was the most supplied parenteral antibacterial in North Macedonia but was ranked fifteenth in Tajikistan and eighteenth in Kyrgyzstan. Ampicillin was ranked third most supplied parenteral agent in Kyrgyzstan and Tajikistan but fifteenth in Armenia.

Table 16. Country rankings of top 20 parenteral antibacterials supplied

AWaRe	ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
Access	J01DB04	Cefazolin	6	–	2	8	–	8	5	2	6
	J01GB03	Gentamicin	–	3	7	18	1	–	15	9	6
	J01XD01	Metronidazole	7	–	4	4	–	4	2	4	6
	J01CA01	Ampicillin	15	–	11	3	–	–	3	8	5
	J01CE01	Benzylpenicillin	8	8	11	–	–	–	19	12	5
	J01CR01	Ampicillin + beta-lactamase inhibitor	15	2	–	8	–	–	8	–	4
Watch	J01DD04	Ceftriaxone	1	1	1	1	2	1	1	1	8
	J01MA02	Ciprofloxacin	5	–	11	5	4	–	6	18	6
	J01DE01	Cefepime	10	11	17	8	–	–	7	15	6
	J01DD01	Cefotaxime	3	12	14	–	–	2	10	7	6
	J01MA12	Levofloxacin	9	–	6	2	–	6	4	6	6
	J01DD02	Ceftazidime	–	9	9	13	–	–	9	17	5
	J01DH02	Meropenem	10	–	8	18	–	–	12	3	5
	J01FF02	Lincomycin	–	10	5	–	2	3	18	–	5
	J01DC02	Cefuroxime	3	–	3	–	–	13	–	–	3
	J01GA01	Streptomycin	–	12	–	–	–	–	–	10	2
Unclassified	J01DD62	Cefoperazone + beta-lactamase inhibitor	–	4	18	–	–	–	–	5	3
	J01CE30	Combinations	10	–	–	–	–	5	–	–	2

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Rankings are reported for agents that were included in the top 10 in two or more countries. This means that in some cases, rankings will be missing because an antibiotic is in the top 10 of only one country. A full list of agents and rankings is shown in Annex 2, Tables A2.1 and A2.2. Agents included in this analysis are: antibacterials for systemic use (J01), neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), rifampicin (J04AB02), rifamycin (J04AB03), rifabutin (J04AB04) and metronidazole (P01AB01). The table is sorted according to the number of countries that included the antimicrobial in their top 20, considering Access (green), Watch (yellow) and unclassified agents (grey) separately *(9)*.

[a] Number of countries that have this agent in their top 20.

3.6.1 Antibacterials supplied by age group

Antibacterials supplied to children and adolescents are shown in Tables 17–19. These define the agents that were included as top five agents in two or more of the participating countries.

Analyses for children under 5 years are limited by the small numbers of encounters reported for this age group. Within this limited data set, the most supplied agents to those aged under 5 years were the Access antibacterial agents amoxicillin + beta-lactamase inhibitor and amoxicillin, and the Watch agent azithromycin (Table 17).

Table 17. Country rankings of top five antimicrobials supplied to children under 5 years

Oral											
AWaRe	ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
Access	J01CR02	Amoxicillin + beta-lactamase inhibitor	1	2	3	1	3	2	1	–	7
	J01CA04	Amoxicillin	2	–	1	1	1	5	–	–	5
	J01DB01	Cefalexin	5	–	–	–	4	–	–	–	2
Watch	J01FA10	Azithromycin	3	3	2	3	2	1	–	1	7
	J01DD08	Cefixime	–	–	4	5	5	3	1	–	5
	J01DC02	Cefuroxime	–	–	–	–	5	4	–	–	2
	J01FA09	Clarithromycin	–	–	–	5	–	–	–	2	2
Parenteral											
AWaRe	ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
Access	J01CA01	Ampicillin	–	–	–	4	–	–	2	–	2
Watch	J01DD04	Ceftriaxone	1	–	–	3	–	–	–	–	2

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Rankings are reported for agents that were included in the top 10 in two or more countries. This means that in some cases, rankings will be missing because an antibiotic is in the top 10 of only one country. Agents included in this analysis are: antibacterials for systemic use (J01), neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), rifampicin (J04AB02), rifamycin (J04AB03), rifabutin (J04AB04) and metronidazole (P01AB01). The table is sorted according to the number of countries that included the antimicrobial in their top five, considering Access (green) and Watch (yellow) agents separately *(9)*.

[a] Number of countries that have this agent in their top five.

The most commonly supplied agents to those aged 5–12 years were the Access agents amoxicillin and amoxicillin + beta-lactamase inhibitor and the Watch agent azithromycin (Table 18).

Table 18. Country rankings of top five antimicrobials supplied to children of 5–12 years

Oral											
AWaRe	ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
Access	J01CA04	Amoxicillin	3	2	1	2	3	4	1	5	8
	J01CR02	Amoxicillin + beta-lactamase inhibitor	1	5	3	3	1	1	–	–	6
	J01CA01	Ampicillin	–	–	–	–	–	5	3	2	3
	J01EE01	Sulfamethoxazole + trimethoprim	4	–	5	5	–	–	–	–	3
Watch	J01FA10	Azithromycin	1	1	2	1	2	2	2	1	8
	J01DD08	Cefixime	5	3	–	–	4	3	–	5	5
	J01MA02	Ciprofloxacin	–	–	5	4	–	–	3	3	4
	J01DC02	Cefuroxime	–	–	4	–	5	–	–	–	2

Table 18 contd

Parenteral											
AWaRe	ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
Access	J01CA01	Ampicillin	–	–	4	4	–	–	1	1	4
	J01DB04	Cefazolin	–	–	2	–	–	–	3	2	3
	J01GB03	Gentamicin	–	–	–	–	1	–	3	–	2
Watch	J01DD04	Ceftriaxone	1	–	1	1	–	–	–	4	4

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Rankings are reported for agents that were included in the top 10 in two or more countries. This means that in some cases, rankings will be missing because an antibiotic is in the top 10 of only one country. Agents included in this analysis are: antibacterials for systemic use (J01), neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), rifampicin (J04AB02), rifamycin (J04AB03), rifabutin (J04AB04) and metronidazole (P01AB01). The table is sorted according to the number of countries that included the antimicrobial in their top five, considering Access (green) + Watch (yellow) agents separately *(9)*.

[a] Number of countries that have this agent in their top five.

Patterns of supply for those aged 13–18 years were broadly like those for younger children. The most commonly supplied oral agents to those aged 13–18 years were the Access antibacterial agents amoxicillin and amoxicillin + beta-lactamase inhibitor and the Watch agent azithromycin (Table 19). The fluoroquinolone ciprofloxacin (Watch agent) was the most supplied oral agent to this age group in Kazakhstan.

Choices of parenteral formulations varied by country. Ceftriaxone (Watch group) was the most supplied parenteral antibacterial in Armenia and the Russian Federation, while ampicillin (Access) was the most supplied in Kyrgyzstan and Tajikistan. Cefazolin (Access) was the most supplied parenteral agent to this age group in Uzbekistan.

Table 19. Country rankings of top five antimicrobials supplied to children of 13–18 years

Oral											
AWaRe	ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
Access	J01CA04	Amoxicillin	3	1	2	1	3	3	1	2	8
	J01CR02	Amoxicillin + beta-lactamase inhibitor	2	3	4	5	2	1	–	–	6
	J01CA01	Ampicillin	–	5	–	5	–	–	4	3	4
	J01AA02	Doxycycline	4	–	–	5	–	5	–	–	3
	J01EE01	Sulfamethoxazole + trimethoprim	4	–	–	–	–	–	3	–	2
Watch	J01FA10	Azithromycin	1	2	3	2	1	2	2	1	8
	J01MA02	Ciprofloxacin	–	–	1	5	4	–	4	4	5
	J01DD08	Cefixime	–	–	–	3	5	–	–	–	2
	J01FA09	Clarithromycin	4	–	–	5	–	–	–	–	2
	J01DD13	Cefpodoxime	–	–	–	5	–	–	–	5	2

Table 19 contd

Parenteral											
AWaRe	ATC	Medicine Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
Access	J01DB04	Cefazolin	–	–	2	2	–	–	4	1	4
	J01CA01	Ampicillin	–	–	2	1	–	–	1	–	3
Watch	J01DD04	Ceftriaxone	1	2	–	2	–	1	2	3	6
	J01MA12	Levofloxacin	2	–	–	2	–	–	–	–	2

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Rankings are reported for agents that were included in the top 10 in two or more countries. This means that in some cases, rankings will be missing because an antibiotic is in the top 10 of only one country. Agents included in this analysis are: antibacterials for systemic use (J01), neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), rifampicin (J04AB02), rifamycin (J04AB03), rifabutin (J04AB04) and metronidazole (P01AB01). The table is sorted according to the number of countries that included the antimicrobial in their top five, considering Access (green) and Watch (yellow) agents separately *(9)*.

[a] Number of countries that have this agent in their top five.

Antibacterial agents supplied to adult customers (above 18 years) are shown in Tables 20–22.

For customers aged 19–35 years, the Watch group agent azithromycin was ranked either most supplied or second most supplied oral agent across all eight country studies (Table 20). Ciprofloxacin (Watch) was the only other agent ranked in the oral top five in all eight country studies.

The Access group agents amoxicillin and amoxicillin + beta-lactamase inhibitor were generally ranked second to fifth in volumes of oral agents supplied across the countries. The Watch group agent ceftriaxone was the most supplied parenteral agent in seven of the eight country studies and ranked third in the remaining country.

Table 20. Country rankings of top five antimicrobials supplied to adults of 19–35 years

Oral											
AWaRe	ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
Access	J01CA04	Amoxicillin	3	3	3	2	5	3	2	4	8
	J01CR02	Amoxicillin + beta-lactamase inhibitor	2	2	4	4	2	1	–	–	6
	P01AB01	Metronidazole	–	–	5	–	–	–	–	3	2
Watch	J01FA10	Azithromycin	1	1	2	1	1	2	1	1	8
	J01MA02	Ciprofloxacin	5	4	1	3	4	5	4	2	8
	J01DD08	Cefixime	–	5	–	–	3	4	–	–	3
	J01MA12	Levofloxacin	–	5	–	4	–	–	5	–	3

Table 20 contd

Parenteral											
AWaRe	ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
Access	J01XD01	Metronidazole	4	–	4	2	–	2	2	–	5
	J01CA01	Ampicillin	4	–	–	5	–	–	3	5	4
	J01DB04	Cefazolin	4	–	2	4	–	–	–	2	4
	J01CE01	Benzylpenicillin	4	4	–	–	–	–	–	–	2
Watch	J01DD04	Ceftriaxone	1	1	1	1	3	1	1	1	8
	J01FF02	Lincomycin	–	–	5	–	3	4	–	–	3
	J01MA02	Ciprofloxacin	3	–	–	5	–	–	4	–	3
	J01MA12	Levofloxacin	–	–	–	3	–	–	5	4	3
	J01DD01	Cefotaxime	4	–	–	–	–	3	–	–	2

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Rankings are reported for agents that were included in the top 10 in two or more countries. This means that in some cases, rankings will be missing because an antibiotic is in the top 10 of only one country. Agents included in this analysis are: antibacterials for systemic use (J01), neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), rifampicin (J04AB02), rifamycin (J04AB03), rifabutin (J04AB04) and metronidazole (P01AB01). The table is sorted according to the number of countries that included the antimicrobial in their top five, considering Access (green) and Watch (yellow) agents separately *(9)*.

[a] Number of countries that have this agent in their top five.

Patterns of supply for those aged 36–60 years were similar to those for customers aged 19–35. The Watch group agent azithromycin was ranked either most supplied or second most supplied oral agent across all eight country studies (Table 21). Ciprofloxacin (Watch) was the only other agent ranked in the oral top five in all eight country studies. The fluoroquinolone levofloxacin (Watch) was included in the top five agents supplied in seven of the eight country studies.

The Access group agents amoxicillin and amoxicillin + beta-lactamase inhibitor were the only Access group agents ranked in the oral top five in more than two countries included in this report. The Watch group agent ceftriaxone was ranked as the most supplied parenteral antibacterial agent across all eight country studies.

Table 21. Country rankings of top five antimicrobials supplied to adults of 36–60 years

Oral											
AWaRe	ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
Access	J01CA04	Amoxicillin	4	–	3	3	–	4	4	–	5
	J01CR02	Amoxicillin + beta-lactamase inhibitor	2	2	–	–	3	2	–	–	4
Watch	J01FA10	Azithromycin	1	1	2	1	1	1	1	1	8
	J01MA02	Ciprofloxacin	5	4	1	1	4	5	5	2	8
	J01MA12	Levofloxacin	3	3	5	4	–	3	2	4	7
	J01FA09	Clarithromycin	–	–	4	–	5	–	–	–	2
Unclassified	J01XX07	Nitroxoline	–	–	–	–	–	–	–	5	1

Table 21 contd

Parenteral											
AWaRe	ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
Access	J01XD01	Metronidazole	5	–	3	5	–	–	2	5	5
	J01DB04	Cefazolin	5	–	2	–	–	–	4	2	4
	J01GB03	Gentamicin	–	5	–	–	3	–	–	–	2
Watch	J01DD04	Ceftriaxone	1	1	1	1	1	1	1	1	8
	J01MA12	Levofloxacin	–	–	4	2	–	5	3	–	4
	J01DC02	Cefuroxime	3	–	4	–	–	–	–	–	2
	J01DD01	Cefotaxime	4	–	–	–	–	2	–	–	2
	J01DE01	Cefepime	–	–	–	5	–	–	5	–	2
Unclassified	J01DD62	Cefoperazone + beta-lactamase inhibitor	–	–	–	–	–	–	–	4	2

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Rankings are reported for agents that were included in the top 10 in two or more countries. This means that in some cases, rankings will be missing because an antibiotic is in the top 10 of only one country. Agents included in this analysis are: antibacterials for systemic use (J01), neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), rifampicin (J04AB02), rifamycin (J04AB03), rifabutin (J04AB04) and metronidazole (P01AB01). The table is sorted according to the number of countries that included the antimicrobial in their top five, considering Access (green), Watch (yellow) and unclassified agents (grey) separately *(9)*.

[a] Number of countries that have this agent in their top five.

Choice of agent supplied for those aged over 60 years was broadly similar to those for other adult customers. The Watch group agent azithromycin was ranked either most supplied or second most supplied oral agent across all eight country studies (Table 22). Ciprofloxacin (Watch) was the only other agent ranked in the oral top five in all eight country studies. The fluoroquinolone levofloxacin (Watch) was included in the top five oral agents supplied in five of the eight country studies. The Access group agents amoxicillin, amoxicillin + beta-lactamase inhibitor and the combination sulfamethoxazole + trimethoprim were the only Access group agents ranked in the oral top five in two or more countries included in this report.

Across the eight studies, parenteral supplies ranged from 0.7% of encounters in North Macedonia to 65.2% in Tajikistan (Table 7). The Watch group agent ceftriaxone was ranked as the most supplied parenteral antibacterial agent in all countries except North Macedonia. More variation was seen across countries in the supply of parenteral antibacterials. Gentamicin was second ranked agent for supply in Georgia, ciprofloxacin was second ranked in Kyrgyzstan and North Macedonia, cefotaxime second ranked in the Russian Federation, cefuroxime second ranked in Kazakhstan, levofloxacin second ranked in Tajikistan and moxifloxacin second ranked in Armenia.

Table 22. Country rankings of top five antimicrobials supplied to adults over 60 years

Oral											
AWaRe	ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
Access	J01CR02	Amoxicillin + beta-lactamase inhibitor	2	2	4	4	4	1	5	–	7
	J01CA04	Amoxicillin	3	–	–	3	5	5	5	–	5

Table 22 contd

Oral											
AWaRe	**ATC**	**Agent**	**Armenia**	**Georgia**	**Kazakhstan**	**Kyrgyzstan**	**North Macedonia**	**Russian Federation**	**Tajikistan**	**Uzbekistan**	**Number of countries[a]**
	J01EE01	Sulfamethoxazole + trimethoprim	–	–	4	–	–	–	3	–	2
Watch	J01FA10	Azithromycin	1	3	2	2	1	2	1	2	8
	J01MA02	Ciprofloxacin	4	5	1	1	3	3	3	3	8
	J01MA12	Levofloxacin	5	1	–	–	–	4	2	4	5
	J01DD08	Cefixime	–	–	–	–	2	–	5	–	2
	J01FA09	Clarithromycin	–	–	–	4	–	–	5	–	2
Parenteral											
AWaRe	**ATC**	**Agent**	**Armenia**	**Georgia**	**Kazakhstan**	**Kyrgyzstan**	**North Macedonia**	**Russian Federation**	**Tajikistan**	**Uzbekistan**	**Number of countries[a]**
Access	J01DB04	Cefazolin	3	–	3	–	–	–	–	3	3
	J01XD01	Metronidazole	–	–	–	–	–	4	4	2	3
	J01GB03	Gentamicin	–	2	–	–	1	–	–	–	2
Watch	J01DD04	Ceftriaxone	1	1	1	1	–	1	1	1	7
	J01MA02	Ciprofloxacin	3	–	–	2	2	–	5	–	4
	J01DD01	Cefotaxime	3	–	3	–	–	2	–	–	3
	J01DH02	Meropenem	3	–	–	4	–	–	3	–	3
	J01MA14	Moxifloxacin	2	–	5	–	–	–	–	4	3
	J01DC02	Cefuroxime	3	–	2	–	–	–	–	–	2
	J01DE01	Cefepime	3	–	–	–	–	–	–	5	2
	J01FF02	Lincomycin	–	–	–	–	3	3	–	–	2
	J01MA12	Levofloxacin	–	–	–	3	–	–	2	–	2

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Rankings are reported for agents that were included in the top 10 in two or more countries. This means that in some cases, rankings will be missing because an antibiotic is in the top 10 of only one country. Agents included in this analysis are: antibacterials for systemic use (J01), neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), rifampicin (J04AB02), rifamycin (J04AB03), rifabutin (J04AB04) and metronidazole (P01AB01). The table is sorted according to the number of countries that included the antimicrobial in their top five, considering Access (green) and Watch (yellow) agents separately *(9)*.

[a] Number of countries that have this agent in their top five.

4. SERBIA

4.1 Methods used in study conducted in Serbia

Most countries of the WHO European Antimicrobial Medicines Consumption network do not have comprehensive systems for collecting and analysing data on medicine purchases, prescriptions and use. Serbia is an exception in that it has an established system of data collection on the reimbursement of medicines, including antimicrobials. Data are generated from dispensing of prescriptions, so a study using the health information system would not be able to capture over-the-counter supplies of antimicrobials without prescription. National enforcement of regulations that require a prescription for supply nevertheless means that very few occasions of sales of antimicrobials without prescription are likely.

Data on supply of antimicrobials for the week of 13–19 April 2020 were extracted from the health information system that collects data on dispensed medicines in all public and 90% of private community pharmacies in Serbia. Given the availability of data from the reimbursement system, patterns of supply of antimicrobials were compared with the same week in 2019 to examine changes in volume and choices of agents prescribed that might be attributable in part to COVID-19 infection.

Information was obtained on dispensed antimicrobials, the age and gender of the patient receiving the antimicrobial, the antimicrobial medicine (including form, strength and quantity supplied), the reported indication for use of the medicine and whether the patient had received more than one antimicrobial agent at the time of the encounter in the pharmacy.

Information on diagnosis/reason for prescription categorized with International Classification of Diseases and Related Health Problems 10th Revision (ICD-10) codes in the health information system was recategorized into the codes defined in the data-collection form shown in Annex 1.

4.2 Description of pharmacies and encounters

Data collection was undertaken for the same one-week period in 2019 and 2020. Public pharmacies represented 15% of the pharmacies included in the study; the remainder were private independent pharmacies (Table 23). Most pharmacies were in urban centres (85% in 2020).

Most notable is the dramatic reduction in numbers of encounters involving supply of antimicrobials in community pharmacies in 2020, falling from 91 964 encounters in 2019 to 30 575 encounters for the comparable period in 2020 (Table 23).

Table 23. Number of included pharmacies and encounters

Year	Total number of pharmacies	Sector			Urban (%)	Rural (%)	Number of encounters recorded nationally
		Public pharmacy	Private chain pharmacy	Private independent pharmacy			
2019	3 696	561 pharmacies 28 167 encounters	NA	3 135 pharmacies 63 822 encounters	87	12	91 964
2020	3 696	561 pharmacies 6 642 encounters	NA	3 135 pharmacies 23 942 encounters	85	15	3 057

NA: not applicable.

4.2.1 Gender and age distribution

While the numbers of encounters fell in 2020, the gender distribution was similar in both years, with more encounters reported for female than male customers (Table 24). This observation is consistent with reporting from most of the other countries participating in the study (see Table 2).

Table 24. Gender distribution of encounters

Year	2019	2020
Number of encounters	91 964	30 575
Female, n (%)	54 259 (59.0%)	17 465 (57.0%)
Male, n (%)	37 705 (41.0%)	13 110 (43.0%)

The age distribution of the recorded encounters in Serbia differed somewhat from that reported in the other eight studies, with more encounters in younger patients (12.6% of encounters included in this study related to those aged 12 years or less (Table 25)). There were relatively fewer encounters in those aged 19–35 years in this study, at 12.5% in 2020 compared to 18.2–46.8% of encounters in the other eight countries (Table 4). Conversely, there were more encounters in those aged over 60 years, at 37% of encounters in 2020; for the other countries, 2.7–26.1% of encounters were in this age group.

In addition to the reduction in numbers of encounters between 2019 and 2020, some differences in the age distribution of encounters were seen. For example, children aged 12 years and less constituted 26.5% of encounters in 2019 but only 12.6% in 2020. A greater number of older patients were included in the 2020 cohort, with 34% aged 36–60 years in 2020 compared to 25.2% in 2019, and 37% aged over 60 years in 2020 compared to 30.8% in 2019.

Table 25. Age distribution of encounters

Year	2019	2020
Total number of encounters	91 964	30 575
< 5 years, n (%)	11 062 (12.0%)	1 872 (6.1%)
5–12 years, n (%)	13 378 (14.5%)	1 985 (6.5%)

Table 25 contd

Year	2019	2020
13–18 years, n (%)	6 282 (6.8%)	1 193 (3.9%)
19–35 years, n (%)	9 787 (10.6%)	3 820 (12.5%)
36–60 years, n (%)	23 172 (25.2%)	10 412 (34.0%)
> 60 years, n (%)	28 283 (30.8%)	11 293 (37.0%)

4.2.2 Description of encounters

There was some variation in the average number of antimicrobials supplied per encounter, from 1.04 antimicrobials per encounter in 2019 to 1.10 in 2020 (Table 26).

The percentage of encounters resulting in supply of more than one antimicrobial doubled from 4.1% in 2019 to 8.6% in 2020.

No encounters in which both oral and parenteral formulations of antimicrobials were supplied were reported, because Serbian law regulates that antibiotics for parenteral use are not dispensed to citizens on prescription in community pharmacies. Parenteral antibiotics are used exclusively in medical institutions and distributed directly to medical settings. There was no information available on duration of supply. A "reason for use" was recorded for all encounters. All encounters were related to presentation of a prescription to a pharmacy.

Table 26. Description of encounters

Year	2019	2020
Number of encounters	91 964	30 575
Number of antimicrobials supplied	96 069	33 541
Average number of antimicrobials per encounter	1.04	1.10
Encounters with more than one antimicrobial supplied, n (%)	3 772 (4.1%)	2 638 (8.6%)
Encounters with supply of both oral and parenteral antimicrobials	0	0
Average days of supply of antimicrobial in days:	NA	NA
oral	NA	NA
parenteral	NA	NA
Encounters where reason for use was recorded	91 964	30 575
Encounters where source of request was recorded:	91 964	30 575
prescription	91 964	30 575
emergency supply	0	0
other	0	0

NA: not available.

4.2.3 Antimicrobial formulations supplied

Across all ATC categories, oral formulations were the most often supplied medicine type, at 86.5% of encounters in 2020 (Table 27). As described above, no supplies of parenteral formulations from community pharmacies were reported in either 2019 or 2020. Other formulation types, including antibacterial eye drops and topical preparations, accounted for 13.5% of supplies in 2020.

Across all encounters, J01 antimicrobial agents were most often supplied, representing 24 848 of 33 541 (74%) supplies of antimicrobials in 2020. J05 and P01 antimicrobials constituted 1361 (4.1%) and 1719 (5.1%) of supplies respectively.

Table 27. Formulation type supplied

	2019	2020
Number of encounters	91 964	30 575
Number of antimicrobials supplied	96 069	33 541
Information on formulation type available (all ATC codes)	96 069	33 541
Oral, n (%)	83 777 (87.2%)	29 005 (86.5%)
Parenteral, n (%)	0 (0.0%)	0 (0.0%)
Other formulation type, n (%)	12 292 (12.8%)	4 536 (13.5%)
J01 antimicrobials supplied	77 378	24 848
Oral, n (%)	77 378 (100.0%)	24 848 (100.0%)
Parenteral, n (%)	0 (0.0%)	0 (0.0%)
J05 antimicrobials supplied	1 613	1 361
Oral, n (%)	1 613 (100.0%)	1 361 (100.0%)
Parenteral, n (%)	0 (0.0%)	0 (0.0%)
P01 antimicrobials supplied	2 548	1 719
Oral, n (%)	2 548 (100.0%)	1 719 (100.0%)
Parenteral, n (%)	0 (0.0%)	0 (0.0%)

Given the relatively smaller numbers of supplies of ATC J05 and P01 antimicrobials, subsequent analyses focus on the J01 group of antibacterials.

With only oral formulations supplied, there were no differences in formulation type by gender or age. Some evidence was found across the other eight studies to suggest differences in formulations of J01 antibacterials supplied according to age, with highest rates of supply of parenteral formulations to customers aged over 60 years (Table 8).

4.3 Indications for treatment

Information on diagnosis/reason for prescription is categorized with ICD-10 codes in the health information system. This information was recategorized into the codes defined in the data-collection form (Annex 1).

Globally, work was undertaken in 2020 to include emergency codes for COVID-19 in ICD-10 and ICD-11 disease classification systems *(11)*. Specifically, in February 2020 emergency codes were activated for a confirmed diagnosis of COVID-19 and a clinical or epidemiological diagnosis (suspected or probable) of COVID-19. The COVID-19 codes were not incorporated into the health information system in Serbia until June 2020, however, so were not being applied by treating physicians at the time this study was conducted. Two reported cases were assigned ICD-10 code B34.2 (coronavirus infection, unspecified).

URTI was the most recorded indication for treatment, comprising 33.3% of cases in 2020 (Table 28). This was nevertheless substantially lower than the reported cases of URTI in 2019 (45.6%). Prescriptions for antimicrobials to treat skin infections were relatively higher in 2020 (10.7% in 2020 versus 6.1% in 2019).

Slightly fewer cases were found in 2020 where influenza was noted as the reason for treatment, but this observation is based on very small numbers. COVID-19 infection was nominated as the indication for treatment in only two cases in 2020. This contrasts with the findings in Armenia, where 1.9% of 2360 encounters were reported as treatment for flu/influenza and 15.3% had COVID-19 nominated as the reason for treatment.

"Other indications" accounted for 28.8% of occasions of supply in 2020.

Table 28. Reported indications for treatment

Indication	2019	2020
URTI, n (%)	41 816 (45.6%)	10 176 (33.3%)
UTI, n (%)	15 809 (17.3%)	6 478 (21.2%)
Gastrointestinal infection, n (%)	3 338 (3.6%)	849 (2.8%)
Skin infection, n (%)	5 592 (6.1%)	3 274 (10.7%)
Eye infection, n (%)	3 559 (3.9%)	990 (3.2%)
Flu/influenza, n (%)	18 (< 0.1%)	10 (< 0.1%)
COVID-19, n (%)	0 (0.0%)	2 (< 0.1%)
Hospital treatment-related, n (%)	0 (0.0%)	0 (0.0%)
"Other indications", n (%)	21 832 (23.8%)	8 796 (28.8%)
Total encounters	**91 646**	**30 575**

4.3.1 Upper respiratory tract infection

A total of 10 176 encounters assigned URTI as a reason for treatment in 2020. Table 29 summarizes the top 10 antibacterial agents supplied for these encounters in 2019 and 2020. The top three agents were consistent across the two years, although the rankings changed. Amoxicillin was the most supplied agent for URTI in 2019 but ranked second in 2020. Azithromycin was ranked third most supplied agent for URTI in 2019 but first in 2020.

Table 29. Rankings of top 10 antimicrobials supplied for the treatment of URTI

ATC	Agent	2019	2020
J01CA04	Amoxicillin	1	2
J01CR02	Amoxicillin + clavulanic acid	2	3
J01FA10	Azithromycin	3	1
J01DB01	Cephalexin	4	4
J01DD08	Cefixime	5	5
J01FA09	Clarithromycin	6	7
J01MA12	Levofloxacin	7	6
J01DB05	Cefadroxil	8	–
J01FA01	Erythromycin	9	8
J01AA02	Doxycycline	10	9
J01FF01	Clindamycin	–	10

4.3.2 Influenza/flu

Only 10 encounters assigned influenza/flu as the reason for treatment in 2020. As such, few antibacterials were reported as supplied for this indication (Table 30).

Table 30. Rankings of top three antimicrobials supplied for the treatment of influenza/flu

ATC	Agent	2019	2020
J01AA02	Doxycycline	1	4
J01DB01	Cephalexin	2	1
J01FA10	Azithromycin	3	–
J01CA04	Amoxicillin	–	1
J01EE01	Sulfamethoxazole + trimethoprim	–	3

4.3.3 UTI

A total of 6478 encounters assigned UTI as a reason for treatment in 2020. Table 31 summarizes the top 10 antibacterial agents supplied for UTI encounters in 2019 and 2020. Rankings were mostly consistent across the two years.

Ciprofloxacin was the most supplied antibacterial for UTI in both 2019 and 2020. Cephalexin ranked second in both years and sulfamethoxazole + trimethoprim ranked third.

Table 31. Rankings of top 10 antimicrobials supplied for the treatment of UTI

ATC	Agent	2019	2020
J01MA02	Ciprofloxacin	1	1
J01DB01	Cephalexin	2	2
J01EE01	Sulfamethoxazole + trimethoprim	3	3
J01MA12	Levofloxacin	4	4
J01XX01	Fosfomycin	5	5
J01MB04	Pipemidic acid	6	–[a]
J01CR02	Amoxicillin + clavulanic acid	7	7

Table 31 contd

ATC	Agent	2019	2020
J01DD08	Cefixime	8	6
J01MA06	Norfloxacin	9	8
J01CA04	Amoxicillin	10	9
J01AA02	Doxycycline	–	10

[a] Marketing authorization for pipemidic acid was withdrawn in 2020.

WHO guidance on the treatment of uncomplicated UTIs suggests that first-choice oral agents for lower UTI are nitrofurantoin, sulfamethoxazole + trimethoprim, trimethoprim, and amoxicillin + clavulanic acid *(6)*. Two of these agents were reported in the top 10 agents used in Serbia for UTI – sulfamethoxazole + trimethoprim was ranked third most supplied while amoxicillin + clavulanic acid was ranked seventh.

WHO suggests first-choice treatment for mild-to-moderate pyelonephritis and prostatitis is ciprofloxacin, with ceftriaxone and cefotaxime as second-choice therapy *(7)*.

4.4 Antimicrobials supplied according to AWaRe classification

The 2019 AWaRe classification of antibiotics includes 180 antibacterial agents (see footnote to Table 32). Table 32 shows the top 20 most supplied oral antibacterials included in the AWaRe classification in 2019 and 2020. While the agents included in the top 20 are essentially the same for the two years, the rankings have changed. In 2020, the top 20 included seven Access agents and 13 agents from the Watch antibiotics. Azithromycin (Watch) was the fourth most supplied agent in 2019 and first ranked in 2020.

Table 32. Rankings of top 20 oral antibacterials supplied

			Ranking	
AWaRe	ATC	Agent	2019	2020
Access	J01CA04	Amoxicillin	1	3
	J01CR02	Amoxicillin + clavulanic acid	2	5
	J01DB01	Cephalexin	3	2
	J01DB05	Cefadroxil	13	19
	J01FF01	Clindamycin	11	10
	J01AA02	Doxycycline	10	9
	J01EE01	Sulfamethoxazole + trimethoprim	9	8
	J01MB04	Pipemidic acid	16	–[a]
Watch	J01FA10	Azithromycin	4	1
	J01MA02	Ciprofloxacin	5	4
	J01DD08	Cefixime	6	6
	J01FA09	Clarithromycin	7	11
	J01MA12	Levofloxacin	8	7
	J01FA01	Erythromycin	12	13
	J01DD13	Cefpodoxime	14	16
	J01XX01	Fosfomycin	15	12
	J01MA06	Norfloxacin	17	14

Table 32 contd

			Ranking	
AWaRe	ATC	Agent	2019	2020
	J01DC10	Cefprozil	18	18
	J01FA06	Roxithromycin	19	17
	J01DC02	Cefuroxime	20	15
	J01MA14	Moxifloxacin	–	20

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Agents included in this analysis are: antibacterials for systemic use (J01), neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), rifampicin (J04AB02), rifamycin (J04AB03), rifabutin (J04AB04) and metronidazole (P01AB01). The table is sorted according to the number of countries that included the antimicrobial in their top 20, considering Access (green) and Watch (yellow) agents separately *(9)*.

[a] Marketing authorization for pipemidic acid was withdrawn in 2020.

4.4.1 AWaRe analyses by age group

Tables 33–38 summarize the rankings of the top 10 antimicrobial agents supplied by age group in 2019 and 2020. The choice of agent in the top 10 remained generally consistent between the two years, with some differences in ranking in 2019 and 2020. The AWaRe classification does not include antiviral agents from the J05 ATC class, so these analyses cannot track changes in relative use of antiviral agents between 2019 and 2020.

The most notable change was that azithromycin (Watch agent) was ranked number one agent supplied for adults over 19 years in 2020 but was ranked fourth in 2019. The Access agents amoxicillin and amoxicillin + clavulanic acid were generally ranked as the first and second most supplied agents across all age groups in 2019, falling slightly in rankings in 2020. The falls were most pronounced in those aged over 60 years, ranking fourth and sixth in 2020.

Table 33. Rankings of the top 10 antimicrobials supplied to children under 5 years

Oral			Ranking	
AWaRe	ATC	Agent	2019	2020
Access	J01CA04	Amoxicillin	1	1
	J01CR02	Amoxicillin + clavulanic acid	2	4
	J01DB01	Cefalexin	4	2
	J01DB05	Cefadroxil	9	8
	J01EE01	Sulfamethoxazole + trimethoprim	10	9
Watch	J01FA10	Azithromycin	3	5
	J01DD08	Cefixime	5	3
	J01DD13	Cefpodoxime	6	7
	J01DC10	Cefprozil	7	6
	J01FA09	Clarithromycin	8	10

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Agents included in this analysis are: antibacterials for systemic use (J01), neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), rifampicin (J04AB02), rifamycin (J04AB03), rifabutin (J04AB04) and metronidazole (P01AB01). The table is sorted according to the number of countries that included the antimicrobial in their top 10, considering Access (green) and Watch (yellow) agents separately *(9)*.

Table 34. Rankings of the top 10 antimicrobials supplied to children of 5–12 years

Oral			Ranking	
AWaRe	ATC	Agent	2019	2020
Access	J01CA04	Amoxicillin	1	1
	J01CR02	Amoxicillin + clavulanic acid	2	2
	J01DB01	Cefalexin	4	3
	J01DB05	Cefadroxil	8	10
	J01EE01	Sulfamethoxazole + trimethoprim	10	6
Watch	J01FA10	Azithromycin	3	4
	J01DD08	Cefixime	5	5
	J01DD13	Cefpodoxime	7	9
	J01DC10	Cefprozil	9	7
	J01FA09	Clarithromycin	6	8

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Agents included in this analysis are: antibacterials for systemic use (J01), neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), rifampicin (J04AB02), rifamycin (J04AB03), rifabutin (J04AB04) and metronidazole (P01AB01). The table is sorted according to the number of countries that included the antimicrobial in their top 10, considering Access (green) and Watch (yellow) agents separately *(9)*.

Table 35. Rankings of the top 10 antimicrobials supplied to adolescents of 13–18 years

Oral			Ranking	
AWaRe	ATC	Agent	2019	2020
Access	J01CA04	Amoxicillin	1	2
	J01CR02	Amoxicillin + clavulanic acid	2	3
	J01DB01	Cefalexin	4	4
	J01DB05	Cefadroxil	7	–
	J01EE01	Sulfamethoxazole + trimethoprim	10	6
	J01FF01	Clindamycin	–	7
Watch	J01FA10	Azithromycin	3	1
	J01DD08	Cefixime	5	5
	J01DD13	Cefpodoxime	9	10
	J01DC10	Cefprozil	–	9
	J01FA01	Erythromycin	8	–
	J01FA09	Clarithromycin	6	8

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Agents included in this analysis are: antibacterials for systemic use (J01), neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), rifampicin (J04AB02), rifamycin (J04AB03), rifabutin (J04AB04) and metronidazole (P01AB01). The table is sorted according to the number of countries that included the antimicrobial in their top 10, considering Access (green) and Watch (yellow) agents separately *(9)*.

Table 36. Rankings of the top 10 antimicrobials supplied to adults of 19–35 years

Oral			Ranking	
AWaRe	ATC	Agent	2019	2020
Access	J01CA04	Amoxicillin	1	2
	J01CR02	Amoxicillin + clavulanic acid	2	3
	J01DB01	Cefalexin	3	4
	J01AA02	Doxycycline	10	10
	J01FF01	Clindamycin	9	7

Table 36 contd

Oral			Ranking	
AWaRe	ATC	Agent	2019	2020
Watch	J01FA10	Azithromycin	4	1
	J01DD08	Cefixime	7	6
	J01FA09	Clarithromycin	5	9
	J01MA02	Ciprofloxacin	6	5
	J01MA12	Levofloxacin	8	8

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Agents included in this analysis are: antibacterials for systemic use (J01), neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), rifampicin (J04AB02), rifamycin (J04AB03), rifabutin (J04AB04) and metronidazole (P01AB01). The table is sorted according to the number of countries that included the antimicrobial in their top 10, considering Access (green) and Watch (yellow) agents separately *(9)*.

Table 37. Rankings of the top 10 antimicrobials supplied to adults of 36–60 years

Oral			Ranking	
AWaRe	ATC	Agent	2019	2020
Access	J01CA04	Amoxicillin	1	2
	J01CR02	Amoxicillin + clavulanic acid	2	5
	J01DB01	Cefalexin	3	3
	J01AA02	Doxycycline	9	–
	J01EE01	Sulfamethoxazole + trimethoprim	10	10
	J01FF01	Clindamycin	–	8
Watch	J01FA10	Azithromycin	4	1
	J01DD08	Cefixime	8	7
	J01FA09	Clarithromycin	6	9
	J01MA02	Ciprofloxacin	5	4
	J01MA12	Levofloxacin	7	6

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Agents included in this analysis are: antibacterials for systemic use (J01), neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), rifampicin (J04AB02), rifamycin (J04AB03), rifabutin (J04AB04) and metronidazole (P01AB01). The table is sorted according to the number of countries that included the antimicrobial in their top 10, considering Access (green) and Watch (yellow) agents separately *(9)*.

Table 38. Rankings of the top 10 antimicrobials supplied to adults over 60 years

Oral			Ranking	
AWaRe	ATC	Agent	2019	2020
Access	J01CA04	Amoxicillin	3	4
	J01CR02	Amoxicillin + clavulanic acid	6	6
	J01DB01	Cefalexin	1	2
	J01AA02	Doxycycline	10	–
	J01EE01	Sulfamethoxazole + trimethoprim	9	7
	J01FF01	Clindamycin	–	9
Watch	J01FA10	Azithromycin	4	1
	J01DD08	Cefixime	8	8
	J01FA09	Clarithromycin	7	10
	J01MA02	Ciprofloxacin	2	3
	J01MA12	Levofloxacin	5	5

Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Agents included in this analysis are: antibacterials for systemic use (J01), neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), rifampicin (J04AB02), rifamycin (J04AB03), rifabutin (J04AB04) and metronidazole (P01AB01). The table is sorted according to the number of countries that included the antimicrobial in their top 10, considering Access (green) and Watch (yellow) agents separately *(9)*.

5. DISCUSSION

Across the eight country studies that used manual data-collection methods, 25 843 community pharmacy encounters in which one or more antimicrobials were supplied during the week of data collection were recorded. Data collection ranged from 1220 encounters in 96 pharmacies in Kyrgyzstan to 9818 encounters in 92 pharmacies in Uzbekistan.

The database study conducted in Serbia was based on much larger numbers of encounters. In total, data were derived from 3696 pharmacies, most of which were in the private sector. Most notable is the substantial reduction in numbers of encounters involving supply of antimicrobials in community pharmacies in 2020, falling from 91 964 encounters in the one-week period in 2019 to 30 575 for the comparable period in 2020. Reasons for the decline between 2019 and 2020 are not entirely clear but may relate to lower numbers of viral infections (URTI and influenza) during the COVID-19 pandemic when citizens were encouraged to stay home, minimize social contacts and, in some places, were subject to stringent lockdown conditions. This hypothesis is supported in part by the observation that recording of URTI as a reason for supply decreased from 45.6% of encounters in 2019 to 33.3% in 2020. Citizens may also have delayed consultations for other health conditions due to the perceived risks of contracting COVID-19.

5.1 Gender and age distribution of encounters

Most countries, including Serbia, reported more encounters with females than males.

The age distribution of clients varied in the eight country studies, but most encounters related to clients aged 19–60 years. Relatively few encounters were recorded for customers aged 12 years or younger – less than 10% of encounters in all countries, except in Kyrgyzstan. Reported encounters for customers aged over 60 years ranged from 2.7% in Kyrgyzstan to 26.1% in North Macedonia. The age differences are difficult to interpret in a study with prospective data collection – pharmacists may have selected specific encounters for recording rather than producing a consecutive series of presentations to the pharmacy.

The age distribution of the database study in Serbia differed from the eight other studies, with more encounters in younger patients, relatively fewer encounters in those aged 19–35 years and more encounters in those aged over 60 years. Some notable changes in presentations between 2019 and 2020 were seen. Some 26.5% of dispensed antimicrobials in 2019 related to children aged 12 years or less, but this fell to 12.6% in 2020. Conversely, dispensing of antimicrobials to those aged 36–60 years increased from 25.2% to 34% and those aged over 60 years from 30.8% to 37% between 2019 and 2020. These observations are consistent with early variants of COVID-19 disease being reported as more severe in older patient groups, leading to infections in this age group possibly being more likely to be treated with antibacterial agents.

5.2 Supply with prescription

The proportion of encounters related to presentation of a prescription ranged from 22.7% of encounters in Tajikistan to 97.1% in North Macedonia. This suggests that over-the-counter supplies

without prescription are occurring in several of the participating countries. Previous studies have highlighted variability in levels of supply of antibacterials without prescription in these countries *(12)*. Other comparative studies are needed to be able to conclude if more than usual levels of supply without prescription were related to the COVID-19 pandemic.

All encounters in Serbia were based on presentation of a prescription as the data are derived from pharmacy dispensing records.

5.3 Antimicrobials supplied

There was little variation in the average number of antimicrobials supplied per encounter across the eight country studies – from 1.01 antimicrobials per encounter in Kazakhstan to 1.55 in Tajikistan. The percentage of encounters resulting in supply of more than one antimicrobial ranged from 0.8% in Kazakhstan to 44.3% in Tajikistan.

In Serbia, the average number of antimicrobials supplied per encounter increased from 1.04 in 2019 to 1.10 in 2020, with the percentage of encounters resulting in supply of more than one antimicrobial doubling from 4.1% in 2019 to 8.6% in 2020.

Supplies of oral and parenteral formulations varied in the eight country studies. Across all ATC categories, oral formulations were the most often supplied medicine type, ranging from 56.3% of encounters in Tajikistan to 99.2% in North Macedonia. Only oral formulations were supplied in Serbia.

Reasons for higher numbers of supplies of parenteral formulations in community pharmacies in Kazakhstan (24.5% of encounters), Kyrgyzstan (31.9%) and Tajikistan (43.7%) are worthy of further investigation to determine if supplies reflect cultural, age or prescriber preferences.

Across all encounters, J01 antimicrobial agents were most often supplied, representing between 61.9% (Russian Federation) and 96% (North Macedonia) of all antimicrobials supplied where information on formulation type was recorded.

Only one country study reported significant numbers of supplies of ATC code J05 antivirals for systemic use – the Russian Federation, with 1194 supplies (26.7% of supplies for which formulation type was reported).

5.4 Influence of gender and age on formulations supplied

There was no evidence to suggest differences in formulations of J01 antibacterials supplied to female and male customers in the country studies. Notably, in the three countries with the highest rates of supply of parenteral formulations (Kazakhstan, Kyrgyzstan and Tajikistan), rates of supply of parenteral formulations were similar for females and males.

Some evidence suggested differences in formulations of J01 antibacterials supplied according to age. In general, supplies of parenteral formulations to younger customers were low, with highest rates of supply to customers aged over 60 years. Country differences were noted, however. In Georgia, for example, parenteral formulations represented 20.4% of J01 supplies, ranging from 5.3% for those aged 13–18 years to 28.5% to those aged over 60 years. In contrast, in Tajikistan, where parenteral forms represented 61.8% of J01 supplies, rates of supply were relatively high across all age groups.

5.5 Indication for treatment

Pharmacists were asked to record a "reason for use" for each encounter – symptoms, a presumptive diagnosis or a confirmed diagnosis. There are many limitations in asking pharmacists the reason for supply, especially when they are supplying medicines based on a prescription written by a medical practitioner and where there is no access to clinical notes and test results. It is likely, however, that discussions between pharmacist and client will reveal some of this information for common conditions.

Pharmacists recorded a "reason for use" in almost all encounters included in the eight country studies.

In Serbia, ICD-10 codes recorded in the health information system were transformed to the categories designated for this study. Notably, ICD-10 codes for confirmed and suspected/probable COVID-19 infection were activated only in February 2020 and not implemented in Serbia until June 2020. The two cases that were recoded as COVID-19 infection were assigned ICD-10 code B34.2 (coronavirus infection, unspecified).

5.5.1 URTI

URTI was the most recorded indication for treatment in each of the eight country studies, ranging from 32.8% of cases in Uzbekistan to 64.5% in Georgia. URTI was the most recorded indication for treatment in the Serbian study at 33.3% of cases in 2020, but this was substantially lower than in 2019 (45.6%).

The most often supplied oral agents for URTI broadly were consistent across countries. Azithromycin was the most frequently supplied agent in five of the eight country studies and was ranked second in a further three countries. Amoxicillin was the only other oral medicine included in the top 10 agents for URTI in all eight countries. The fluoroquinolones ciprofloxacin and levofloxacin were included in the top 10 agents in six and seven countries respectively. The antiviral agent umifenovir was included in the top 10 agents for URTI in three countries.

In Serbia, the top three agents were consistent across 2019 and 2020, although the rankings changed. Amoxicillin was most supplied agent for URTI in 2019 but ranked second in 2020. Azithromycin was ranked as the third most supplied agent for URTI in 2019 but first in 2020. Levofloxacin was the only fluoroquinolone included in the top 10 agents for URTI and was ranked as the sixth most supplied agent in 2020.

The draft WHO Essential Medicines List Antibiotic Book *(6)* does not recognize URTI as a single clinical condition. Bronchitis and pharyngitis are related common presentations in primary care. The draft book describes acute bronchitis as usually presenting as a persistent cough with or without mild fever, noting that virtually all cases are viral and self-limiting and that antibiotics are not needed in most instances. Similarly, sore throat (pharyngitis) is cited as one of the most common conditions in patients presenting to primary health care and a very frequent cause of inappropriate antibiotic prescribing, with up to 60% of patients with sore throat in many high-income outpatient settings given antibiotics. The book states that most cases of pharyngitis are of viral origin and do not benefit from antibiotics.

Results here suggest that cases of URTI are commonly treated with antibiotics. It is difficult to draw firm conclusions, however, as the encounters reported in the studies were occasions of supply of antimicrobial agents. There is no information on presentations with URTI where no antibiotic was supplied or on the severity of infections treated.

5.5.2 UTI

There were 3564 occasions of UTI-related supply of antimicrobials, ranging from 8.6% of encounters in Armenia to 25.7% in Georgia. Eighteen oral and 15 parenteral agents were reported as being supplied for UTI. Oral forms of the fluoroquinolones ciprofloxacin and levofloxacin were included in the top 10 agents in all eight countries, with ciprofloxacin ranked first in five countries, second in one country and third in one country. Two other fluoroquinolones, norfloxacin and ofloxacin, were also included in five and two countries respectively.

In Serbia, ciprofloxacin was the most supplied antibacterial for UTI in both 2019 and 2020, with cephalexin ranked second in both years and sulfamethoxazole + trimethoprim ranked third. Two other fluoroquinolones, levofloxacin and norfloxacin, were included in the top 10 agents for UTI, ranked as the fourth and sixth most supplied agents in 2020.

WHO guidance on the treatment of uncomplicated UTIs suggests that first-choice oral agents for lower UTI are nitrofurantoin, sulfamethoxazole + trimethoprim, trimethoprim, and amoxicillin + clavulanic acid *(6)*. These agents were included in the top 10 analyses in two, four, zero and five countries respectively. Nitroxoline (J01XX07) and furazidin (J01XE03) are closely related to nitrofurantoin and each of these agents was included in the top 10 for three countries. It should be noted that amoxicillin was removed as a first-line agent for UTI in the 2021 revision of the WHO Model List of Essential Medicines *(13)*.

The extensive use of fluoroquinolones such as ciprofloxacin and levofloxacin for UTI is a potential concern. The European Medicines Agency (EMA) reviewed medicines containing fluoroquinolone and quinolone antibiotics in 2018 *(14)*. In addition to recommending suspension of the marketing authorization for medicines containing cinoxacin, flumequine, nalidixic acid and pipemidic acid, EMA's Committee for Medicinal Products for Human Use (CHMP) recommended restricting the use of the remaining fluoroquinolone antibiotics. The CHMP recommended restrictions on the use of fluoroquinolones, advising that they should not be used to:

- treat infections that might get better without treatment or are not severe (such as throat infections);
- treat non-bacterial infections (such as non-bacterial (chronic) prostatitis);
- prevent traveller's diarrhoea;
- prevent recurring lower UTIs (urine infections that do not extend beyond the bladder); or
- treat mild or moderate bacterial infections unless other antibacterial medicines commonly recommended for these infections cannot be used.

The results of the country studies suggest there are opportunities to review national guidance on the management of UTIs to ensure recommendations align with best-practice international guidelines. In particular, the use of fluoroquinolones should be reviewed.

5.5.3 COVID-19 infections

There were 2064 occasions of supply of antimicrobials related to COVID-19-related reasons, ranging from 0.5% of encounters reported in Georgia to 15.3% in Armenia. Only two cases of COVID-19-related supply were recorded in Serbia. Thirteen oral agents and eight parenteral agents were included in the top 10 agents across the country studies for this indication. The fluoroquinolone levofloxacin was the

only oral agent included in the top 10 in all eight countries and was ranked first in two. Azithromycin was first-ranked agent in five countries but was not included in the top 10 agents in Georgia.

Early in the pandemic, azithromycin was proposed as a treatment for COVID-19, with in vitro studies suggesting activity against some viruses, including severe SARS-CoV-2 *(3,4)*. Subsequently, a United Kingdom-based randomized controlled trial (the PRINCIPLE trial) conducted in primary care assessed the benefits of azithromycin treatment in people aged 65 years and older, or those who were 50 years and older with at least one comorbidity and had been unwell for 14 days or less with suspected COVID-19 infection *(15)*. The trial 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. This evidence was not published until March 2021, after this study was completed.

Two antiviral agents were included in the top 10 – umifenovir, included in the top 10 for five countries, and oseltamivir, two countries. Umifenovir was ranked as the most supplied oral agent in Kyrgyzstan, while oseltamivir was ranked first in Kazakhstan. The choices are consistent with COVID-19 infection being viral.

Hydroxychloroquine was ranked second for supply in Georgia and Uzbekistan. As noted by Jorge *(5)*, early in the pandemic, hydroxychloroquine was suggested as a possible prevention method or treatment for COVID-19, given evidence of in vitro inhibition of SARS-CoV-2 *(16)*. Multiple high-quality studies subsequently showed no benefit of hydroxychloroquine use as post-exposure prophylaxis or as a COVID-19 treatment *(17)*. Studies of the use of hydroxychloroquine in the prevention of COVID-19 mortality were similarly negative *(18)*.

5.5.4 Influenza/flu

Treatments for influenza/flu are of interest, as it may not have been possible to distinguish influenza and COVID-19 symptoms early in the course of disease. There were 2230 occasions of supply where influenza/flu was the reported reason for treatment, with 20 oral medicines included in the top 10 agents across the eight country studies.

Consistent with its widespread use for URTI and COVID-19-related infections, azithromycin was the most supplied oral J01 agent. It was included in the top 10 for six countries and ranked first in three.

There were seven antiviral agents and one categorized as "other immunostimulants". The antiviral agents were inosine pranobex, included in the top 10 for five countries, umifenovir (five countries), aciclovir (five), tilorone (three), "other antivirals" (three), rimantadine (two) and oseltamivir (two).

5.6 AWaRe

Analyses based on the AWaRe classification are more limited, in that not all antimicrobial agents are included in the classification. This is particularly relevant for this study, as AWaRe does not include antiviral agents. The results of the eight country studies and the study in Serbia nevertheless confirm widespread use of antibiotics for the management of URTI, UTI, COVID-19 and influenza. The choice of antibacterial agent therefore is important.

Antibiotics from the Access group have a narrow spectrum of activity, lower cost, a good safety profile and generally low resistance potential and are recommended as empiric first- or second-choice treatment options for common infections. Watch antibiotics are broader-spectrum antibiotics, generally with higher costs, and are recommended only as first-choice options for patients with more

severe clinical presentations or for infections where the causative pathogens are more likely to be resistant to Access antibiotics (such as URTIs). Reserve antibiotics are last-choice antibiotics used to treat multidrug-resistant infections.

Only three agents were included in the top 10 for supplies in all eight country studies – amoxicillin (Access agent), azithromycin and ciprofloxacin (Watch group agents). An additional two agents – amoxicillin + beta-lactamase inhibitor (Access agent) and levofloxacin (Watch) – were reported in the top 10 agents for supply in seven of the eight country studies.

Across all indications, the Watch group agent azithromycin was ranked either most supplied or second most supplied agent across all eight country studies. This pattern was reasonably consistent across all age groups except children under 12 years. The Access group agents amoxicillin and amoxicillin + beta-lactamase inhibitor generally were ranked second to ninth in volumes of supply across the countries and across all age groups. Concerns about the widespread supply of fluoroquinolones (Watch agents), including ciprofloxacin and levofloxacin, have been described above. The Watch agent ceftriaxone was the most widely supplied parenteral antimicrobial across indications and age groups.

The study in Serbia allowed an assessment of changes in prescribing choices between 2019 and 2020. While the choices of agent in the top 10 remained generally consistent between the two years, there were some differences in rankings. The most notable change was that azithromycin (Watch agent) was ranked number one agent supplied for adults over 19 years in 2020; it had been ranked fourth in 2019. The Access agents amoxicillin and amoxicillin + clavulanic acid generally were ranked as the first and second most supplied agents across all age groups in 2019, falling slightly in rankings in 2020.

These findings suggest there are further opportunities to promote the AWaRe classification as a tool to guide national stewardship efforts to promote responsible use of antibiotics and slow the spread of antibiotic resistance. The aim is to increase use of narrow-spectrum antibiotics and reduce use of broad-spectrum agents. WHO's Thirteenth General Programme of Work 2019–2023 includes a target of at least 60% of total antibiotic prescribing at country level being Access antibiotics by 2023 *(19,20)*.

6. CONCLUSIONS

The studies reported here illustrate the value of a review of prescribing and dispensing practices, in this case for antimicrobial agents supplied in the context of the COVID-19 pandemic. In the absence of electronic systems, manual data-collection methods in community pharmacies can be used to collect information that can inform understanding of how the medicines are used in practice.

Overall, the trends were towards increased use of medicines that had been proposed for the treatment for COVID-19 infection, specifically azithromycin and, to a lesser extent, hydroxychloroquine. Azithromycin, however, was the most supplied agent across a range of clinical indications, not just presumed or confirmed COVID-19 infection. There was no information available on national or local shortages of antibiotics at the time the country studies were conducted, so it is not possible to know how shortages may have influenced the choice of antibiotic supplied. However, the widespread use of azithromycin shown in these studies occurred during the period of increased global demand for the antibiotic.

While the data on indication for treatment may not always be robust, presumptive diagnoses will influence treatment choices and the data will reflect patterns of supply in community pharmacies. Consistency in findings across the studies tends to support the validity of individual country results. Country differences in treatment choices nevertheless were noted, illustrated by differences in the rankings of supply of specific agents. Countries also varied in the extent of use of antiviral agents. The reasons for these differences are worthy of further investigation.

Reasons for the high levels of use of azithromycin, a Watch agent, across many different clinical indications should be examined in more detail. Suboptimal practices, such as inappropriate prescribing choices for specific clinical indications and/or overreliance on Watch group antibiotics, can be identified and interventions developed to address them.

The database study in Serbia illustrates the enhanced value of electronic records. Large datasets over different time periods can be assembled easily, quickly and at low cost. The scope of such analyses is limited by the data fields available and the validity and reliability of diagnostic codes assigned in the system, but the ability to monitor changes over time is a particular strength of database studies. As countries in the WHO European Region develop their medicines reimbursement programmes, increasing opportunities will arise to use the data collected on medicines dispensed and indications for treatment for research purposes and to monitor the quality of care being provided.

The studies reported here have some limitations. To an extent, the data from the eight country studies is self-reported, but use of practising pharmacists and a standard data-collection tool should help ensure the collection of valid and reliable data. In addition, local study coordinators from the research group engaged to conduct the study in-country will have conducted regular supervision of the pharmacists and reviewed the adequacy of the data collection. It is unclear whether the reported encounters represent a consecutive series of presentations to the pharmacy or were selected by the pharmacist for inclusion in the study.

The findings of the country studies that include regional analyses and results of the crossnational analyses presented in this report can be used to review issues around access to, and appropriate choices of, antibacterial agents for common presentations in community care.

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ANNEX 1. DATA-COLLECTION FORM

Antimicrobial agents supplied in community pharmacies data-collection form

Fill in the data on antimicrobial (antibiotic, antifungal, antimalarial, antiviral) medicines supplied to customers/clients of the pharmacy. Each customer/client has an encounter number: 1 for the first client, 2 for the second client, and so on. Where more than one antimicrobial is supplied to a customer during a visit, use two (or more) lines to record supplies using a single encounter number.

FORM: O (oral tablet, capsule, powder, liquid, granules); **I** (injection); **R** (rectal formulation); **X** other formulation type.

REASON FOR USE: use codes A to F or enter text for any other reason for use:

A. Upper respiratory tract infection	**D**. Skin infection	**G**. COVID-19
B. Urinary tract infection	**E**. Eye infection	**H**. Hospital use
C. Gastrointestinal infection	**F**. Flu/influenza	**O**. Other

SOURCE OF REQUEST: P (prescription written by a health care professional), **E** (emergency supply*), **O** (other)

*Emergency supply defined by law, e.g., in case of emergency needs during the time doctors' consultation is not available.

Country: _____ **Pharmacy location**: ☐ Urban ☐ Rural

Pharmacy ownership: ☐ Public ☐ Private: if private ☐ Chain ☐ Independent

Encounter number (each client has a new number)	Date of supply	Details of antimicrobial supplied				Patient		Reason for use	Source of request use codes
		Name of medicine (INN)	Form	Daily dose (mg)[a]	Days of supply[b]	Age	Sex (F/M)	Use codes A–O If O (Other), please specify	

F: female. INN: International Nonproprietary Names. M: male.

[a] Strength of medicine was recorded for Armenia, Kyrgyzstan, the Russian Federation and Uzbekistan.

[b] Supplied quantity was recorded for Armenia, Kyrgyzstan, the Russian Federation and Uzbekistan.

ANNEX 2. ANALYSIS OF SUPPLY OF ORAL AND PARENTERAL ANTIBACTERIALS

Table A2.1 shows country rankings of the top 20 oral antibacterials supplied and Table A2.2 presents the top 20 parenterals supplied.

Table A2.1. Country rankings of top 20 oral antibacterials supplied

AWaRe	ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
Access	J01CA04	Amoxicillin	3	4	3	2	5	3	3	7	8
	P01AB01	Metronidazole	11	13	6	7	18	9	9	3	8
	J01AA02	Doxycycline	6	8	11	9	13	8	16	–	7
	J01CR02	Amoxicillin + beta-lactamase inhibitor	2	2	4	4	3	1	9	–	7
	J01EE01	Sulfamethoxazole + trimethoprim	8	–	10	8	17	13	4	20	7
	J01CA01	Ampicillin	–	11	14	13	–	19	13	5	6
	J01BA01	Chloramphenicol	19	14	19	–	–	–	14	–	4
	J01AA07	Tetracycline	16	–	–	15	–	–	6	–	3
	J01XE01	Nitrofurantoin	20	–	–	20	–	18	–	–	3
	J01DB01	Cefalexin	18	–	–	–	8	–	–	–	2
	J01FF01	Clindamycin	17	–	–	–	9	–	–	–	2
	J01EE04	Sulfamoxole + trimethoprim	–	7	–	–	–	–	–	–	1
Watch	J01DD08	Cefixime	7	6	12	13	2	6	19	15	8
	J01FA09	Clarithromycin	10	18	8	6	7	7	8	9	8
	J01FA10	Azithromycin	1	1	2	1	1	2	1	1	8
	J01MA02	Ciprofloxacin	5	5	1	3	4	5	5	2	8
	J01MA12	Levofloxacin	4	3	7	5	14	4	2	4	8
	J01MA06	Norfloxacin	15	–	13	12	11	11	–	17	6
	J01DC02	Cefuroxime	13	–	5	–	6	14	–	–	4
	J01DD13	Cefpodoxime	–	19	14	–	16	–	–	19	4
	J01FA02	Spiramycin	–	–	14	10	18	–	–	16	4
	J01MA14	Moxifloxacin	8	16	–	–	10	–	–	18	4
	J01FA01	Erythromycin	–	9	–	10	–	–	6	–	3
	J01FA03	Midecamycin	12	–	–	18	15	–	–	–	3
	J01FA06	Roxithromycin	–	–	–	20	–	–	20	10	3
	J01FA07	Josamycin	14	–	18	–	–	10	–	–	3
	J01MA01	Ofloxacin	–	–	14	–	–	–	11	8	3

Table A2.1 contd

AWaRe	ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
	J01XX01	Fosfomycin	–	14	9	–	–	12	–	–	3
	A07AA11	Rifaximin	–	–	–	–	–	16	–	–	1
	J01DC04	Cefaclor	–	–	–	–	18	–	–	–	1
	J01DD15	Cefdinir	–	10	–	–	–	–	–	–	1
	J01DE01	Cefepime	–	–	–	–	–	–	16	–	1
	J01FF02	Lincomycin	–	–	–	–	–	16	–	–	1
	J01MA03	Pefloxacin	–	–	–	–	–	–	–	13	1
	J04AB02	Rifampicin	–	–	–	–	–	–	–	10	1
Unclassified	J01XE03	Furazidin	–	12	–	–	–	15	15	14	4
	J01XX07	Nitroxoline	–	19	–	18	–	–	11	6	4
	J01RA12	Ciprofloxacin + ornidazole	–	16	–	15	–	–	–	–	2
	J01XD03	Ornidazole	–	–	–	–	–	–	16	12	2
	J01CE10	Benzathine phenoxymethylpenicillin	–	–	–	–	12	–	–	–	1
	J01FA11	Miocamycin	–	–	19	–	–	–	–	–	1
	J01XD02	Tinidazole	–	–	–	–	–	–	20	–	1
	J01XE02	Nifurtoinol	–	–	–	15	–	–	–	–	1
	J01RA11	Ciprofloxacin + tinidazole	–	–	–	–	–	20	–	–	1

ATC: Anatomical Therapeutic Chemical (categories).
AWaRe: (WHO) Access, Watch, Reserve (classification).
Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Agents included in this analysis are: antibacterials for systemic use (J01), neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), rifampicin (J04AB02), rifamycin (J04AB03), rifabutin (J04AB04) and metronidazole (P01AB01).
The table is sorted according to the number of countries that included the antimicrobial in their top 20, considering Access (green), Watch (yellow) and unclassified agents (grey) separately *(1)*. European Union/European Economic Area population-weighted mean for countries of the European Surveillance of Antimicrobial Consumption Network. WHO/Antimicrobial Medicines Consumption population-weighted mean for countries of the WHO Europe Antimicrobial Medicines Consumption Network.
[a] Number of countries that have this agent in their top 20.

Table A2.2. Country rankings of top 20 parenteral antibacterials supplied

AWaRe	ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
Access	J01DB04	Cefazolin	6	–	2	8	–	8	5	2	6
	J01GB03	Gentamicin	–	3	7	18	1	–	15	9	6
	J01XD01	Metronidazole	7	–	4	4	–	4	2	4	6
	J01CA01	Ampicillin	15	–	11	3	–	–	3	8	5
	J01CE01	Benzylpenicillin	8	8	11	–	–	–	19	12	5
	J01GB06	Amikacin	10	5	15	–	–	–	13	11	5
	J01CA04	Amoxicillin	–	–	18	15	4	13	–	–	4
	J01CR01	Ampicillin + beta-lactamase inhibitor	15	2	–	8	–	–	8	–	4
	J01CR02	Amoxicillin + beta-lactamase inhibitor	10	–	–	7	–	11	–	–	3
	J01BA02	Thiamphenicol	–	–	20	–	–	9	–	–	2

Table A2.2 contd

AWaRe	ATC	Agent	Armenia	Georgia	Kazakhstan	Kyrgyzstan	North Macedonia	Russian Federation	Tajikistan	Uzbekistan	Number of countries[a]
	J01CE08	Benzathine benzylpenicillin	–	14	–	–	–	13	–	–	2
	J01AA07	Tetracycline	–	–	–	11	–	–	–	–	1
	J01CF04	Oxacillin	–	–	–	–	–	–	–	16	1
	J01FF01	Clindamycin	–	–	–	–	4	–	–	–	1
Watch	J01DD04	Ceftriaxone	1	1	1	1	2	1	1	1	8
	J01MA02	Ciprofloxacin	5	–	11	5	4		6	18	6
	J01DE01	Cefepime	10	11	17	8	–	–	7	15	6
	J01DD01	Cefotaxime	3	12	14	–	–	2	10	7	6
	J01MA12	Levofloxacin	9	–	6	2	–	6	4	6	6
	J01DD02	Ceftazidime	–	9	9	13	–	–	9	17	5
	J01DH02	Meropenem	10	–	8	18	–	–	12	3	5
	J01FF02	Lincomycin	–	10	5	–	2	3	18	–	5
	J01MA01	Ofloxacin	–	–	9	13	–	–	14	20	4
	J01MA14	Moxifloxacin	2	–	15	15	–	–	–	19	4
	J01DD12	Cefoperazone	15	–	20	–	–	–	–	14	3
	J01DC02	Cefuroxime	3	–	3	–	–	13	–	–	3
	J01GA01	Streptomycin	–	12	–	–	–	–	–	10	2
	J01FA10	Azithromycin	–	–	–	17	–	9	–	–	2
	J01XX01	Fosfomycin	–	–	–	18	–	6	–	–	2
	J01FA09	Clarithromycin	–	–	–	–	–	–	–	13	1
	A07AA08	Kanamycin	–	–	–		–	–	19	–	1
	J01DD08	Cefixime	–	–	–	6	–	–	–	–	1
	J01FA07	Josamycin	–	–	–	–	–	13	–	–	1
	J01GB04	Kanamycin	15	–	–	–	–	–	–	–	1
	J01XA01	Vancomycin	–	6	–	–	–	–	–	–	1
	J01DH03	Ertapenem	–	–	20	–	–	–	–	–	1
Unclassified	J01DD62	Cefoperazone + beta-lactamase inhibitor	–	4	18	–	–	–	–	5	3
	J01CE30	Combinations	10	–	–	–	–	5	–	–	2
	J01DD63	Ceftriaxone + beta-lactamase inhibitor	–	7	–	12	–	–	–	–	2
	J01CA51	Ampicillin, combinations	–	–	–	–	–	–	16	–	1
	J01CR50	Combinations of penicillins	–	–	–	–	–	–	16	–	1
	J01DD54	Ceftriaxone, combinations	–	–	–	–	–	–	10	–	1
	J01XX	Other antibacterials	–	–	–	–	–	11	–	–	1

ATC: Anatomical Therapeutic Chemical (categories).
AWaRe: (WHO) Access, Watch, Reserve (classification).
Note: the numbers shown refer to the frequency of use: for example, 1 = most often supplied antimicrobial. Agents included in this analysis are: antibacterials for systemic use (J01), neomycin (A07AA01), streptomycin (A07AA04), polymyxin B (A07AA05), kanamycin (A07AA08), vancomycin (A07AA09), colistin (A07AA10), rifamixin (A07AA11), rifampicin (J04AB02), rifamycin (J04AB03), rifabutin (J04AB04) and metronidazole (P01AB01). The table is sorted according to the number of countries that included the antimicrobial in their top 20, considering Access (green), Watch (yellow) and unclassified agents (grey) separately *(1)*.
[a] Number of countries that have this agent in their top 20.

Reference

1. WHO releases the 2019 AWaRe classification antibiotics. In: World Health Organization [website]. Geneva: World Health Organization; 2019 (https://www.who.int/news/item/01-10-2019-who-releases-the-2019-aware-classification-antibiotics, accessed 7 March 2022).

The WHO Regional Office for Europe

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