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

AMC data 2011–2017
EXECUTIVE SUMMARY
Abstract

WHO Regional Office for Europe Antimicrobial Medicines Consumption (AMC) Network: AMC data 2011–2017 is the second WHO Europe AMC Network report. It updates analyses of data on antimicrobial medicines consumption collected for the period from 2011 to 2017 from non-European Union countries and areas in the WHO European Region. The update includes analyses of trends over time for key metrics of antibiotic consumption, considers new metrics to inform the responsible use of antibiotics and examines the impact of changes to defined daily doses that came into force on 1 January 2019. The WHO Regional Office for Europe and its partners remain committed to supporting countries and areas in these endeavours through the activities of the WHO Europe AMC Network. This executive summary describes the methodology and highlights key findings from the report.

Keywords

ANTIMICROBIAL MEDICINES CONSUMPTION
NATIONAL SURVEILLANCE NETWORKS
ANTI-INFECTIVE AGENTS – THERAPEUTIC USE
ANTIBIOTICS
EPIDEMIOLOGICAL MONITORING
DATA COLLECTION
RESPONSIBLE USE OF ANTIBACTERIALS
EASTERN EUROPE AND CENTRAL ASIA

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ISBN: 9789289054751

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ACKNOWLEDGEMENTS

The WHO Regional Office for Europe would like to thank the WHO Europe Antimicrobial Medicines Consumption (AMC) Network members for providing antimicrobial consumption data and for their valuable contributions to the report from which this executive summary is drawn.

The WHO Regional Office for Europe would also like to acknowledge the European Centre for Disease Prevention and Control, specifically Dr Klaus Weist and Dr Dominique Monnet, for their ongoing support and valued collaboration.

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

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WHO Europe AMC Network activities are coordinated by the WHO Regional Office for Europe. The financial support of the Ministry of Health, Welfare and Sport of the Netherlands and the German Collaboration Programme are gratefully acknowledged.
ABBREVIATIONS

AMC  antimicrobial medicines consumption
ATC  Anatomical Therapeutic Chemical (classification system)
AWaRe WHO Access, Watch and Reserve (classification)
DDD  defined daily dose
DID  defined daily doses per 1000 inhabitants per day
ECDC European Centre for Disease Prevention and Control
ESAC-Net European Surveillance of Antimicrobial Consumption Network

Abbreviations of country names used in figures

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

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

Albania, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Georgia, Kazakhstan, Kyrgyzstan, Montenegro, North Macedonia, the Republic of Moldova, the Russian Federation, Serbia, Tajikistan, Turkey, Ukraine and Uzbekistan, as well as Kosovo, are members of the WHO Europe AMC Network.

*WHO Regional Office for Europe Antimicrobial Medicines Consumption (AMC) Network: AMC data 2011–2017* is the second WHO Europe AMC Network report. It sets out and analyses AMC data for 16 of the participating countries as well as for Kosovo in which the ministry of health and public health authorities approved data-sharing and publication. The report includes analyses of trends over time (2011–2017) for key metrics of antibacterial consumption, applies the 2017 WHO Core Access, Watch and Reserve classification of antibiotics, and examines the impact of proposed changes to defined daily doses (DDDs) in 2019 for some commonly used antibiotics. Results are compared with ESAC-Net quality indicator estimates for 2017. Analyses are presented for each AMC Network country and area separately, with comparisons across the AMC Network for selected metrics.

**Methodology**

The report builds on the early experience of data collection at country and area levels. It provides an analysis of data collected between 2011 and 2017 and includes several comparisons across the AMC Network for selected measures. The results mainly relate to analyses of antimicrobials for systemic use (Anatomical Therapeutic Chemical (ATC) group J01). Most countries and areas participating in the WHO Europe AMC Network use import data (from customs records and declaration forms) as the source of information on antimicrobial consumption. These are supplemented with sales records from market authorization holders or local manufacturing estimates where there is local pharmaceutical manufacturing. In some cases, data from wholesalers are used. Increasingly, data on antimicrobial use are available from health insurance programmes.

In most of the countries and areas participating in the WHO Europe AMC Network, it is not possible to disaggregate data by sector (community or hospital; public or private), so total consumption data are reported in most cases. Analyses are also reported by community and hospital sectors separately where disaggregated data are available. The WHO Europe AMC Network uses the ATC classification system, and the most commonly used measurement metric is the number of DDDs/1000 inhabitants per day (DID). Data for ATC category J01 are analysed to give country- or area-specific trends in antimicrobial consumption and trends across the AMC Network.

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1 All references to Kosovo in this publication should be understood to be in the context of United Nations Security Council resolution 1244 (1999).
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. This classification could support antimicrobial stewardship efforts and focus attention on prescribing practices that should be reviewed further.

The **Access** group includes first- and second-choice antibiotics that should be widely available in all countries and areas. They should be affordable and quality-assured.

The **Watch** group includes antibiotic classes that generally are considered to have higher resistance potential and which remain recommended as first- or second-choice treatments but for a limited number of indications. The group includes the highest-priority agents on the critically important antibiotics list (World Organisation for Animal Health 2015; WHO, 2017a) and/or antibiotics that are at relatively high risk of selection of bacterial resistance. These medicines should be “prioritized as key targets of local and national stewardship programmes and monitoring” (WHO, 2017b).

The **Reserve** group of antibiotics includes antibiotics and antibiotic classes that the Expert Committee considered as last-resort agents, that is, those to be used when other alternatives would be inadequate or have already failed in, for example, serious life-threatening infections due to multidrug-resistant bacteria.

It is therefore useful to monitor the relative use of these classes of agents that should be used sparingly and judiciously to preserve their value for clinical medicine.

In October 2017, the WHO International Working Group for Drug Statistics Methodology recommended changes to the DDDs for seven commonly used antibiotics (mainly penicillins) and endorsed new DDDs for oral colistin along with changes for several other products (WHO Collaborating Centre for Drug Statistics Methodology, 2018). The changes were requested given evidence that current DDD allocations for commonly used medicines differed substantially from recommended doses and doses used in clinical practice. The DDD changes have been adopted fully since January 2019 and will affect estimates of total AMC and relative use of classes of antibiotics. The interpretation of national estimates and comparisons across the AMC Network over time will need to take account of these changed DDD values.

The report focuses on five types of key measure used to examine trends over time:

- volume of consumption measures, reported as numbers of DID using DDD values relevant to the specific year of data (2011–2017) then applying the DDD values implemented in January 2019;
- relative consumption measures, expressed as a percentage of total consumption of a group of antimicrobials;
- the agents consumed, reflecting the choice of specific antimicrobial agents within a class and allowing more focused assessment of whether the choices align with recommended best practices and clinical practice guidelines;
- consumption according to the 2017 WHO AWaRE group classification (WHO Access, Watch and Reserve (classification)); and
- utilization of the 10 most consumed agents (oral and parenteral agents separately).
Key findings

Data on total consumption of antibacterials for systemic use (ATC classification group J01) were available for 16 countries as well as for Kosovo. There was large variability in reported consumption of J01 antibacterials across the AMC Network – ranging from 8.5 DID (Azerbaijan) to 36.4 DID (Turkey) in 2017. The population-weighted mean consumption across the 17 datasets was 21.1 DID (median consumption 20.3 DID).

These consumption estimates were mostly lower than those reported in 2011 (range 6.4 DID for Uzbekistan to 42.3 DID for Turkey, mean 23.6 DID) and in 2015 (range 8.0 DID for Azerbaijan to 41.5 DID for Turkey, mean 21.2 DID). ESAC-Net analyses also show considerable variability in total J01 consumption, ranging from 11.0 DID in the Netherlands to 34.1 DID in Spain in 2017 (ECDC, 2018) (Fig. ES1).

The extent of consumption of parenteral formulations also varied widely – 4% in Turkey and 5% in Bosnia and Herzegovina, up to 45% in Kyrgyzstan and 50% in Uzbekistan in 2017.

The most commonly consumed subgroup of antibacterials was beta-lactams (ATC group J01C), with a range of 28% (Kazakhstan) to 52.5% (Uzbekistan) of total J01 consumption in 2017. Cephalosporins (J01D) represented between 9% (Armenia) and 27.5% (Uzbekistan) of J01 consumption; quinolones (J01M) made up 22.9% of J01 consumption in Tajikistan.

Choice of cephalosporins varied widely in 2017. Overall, consumption of fourth-generation agents was limited (mostly < 0.1 DID). Consumption of first-generation agents varied from very low in Azerbaijan to 59% of total cephalosporin consumption in Serbia, and second-generation agents from very low consumption (< 0.1 DID) in several settings to 51% of cephalosporin consumption (4.9 DID)

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in Turkey. Third-generation agent consumption ranged from 22% (Bosnia and Herzegovina) to 88% (Azerbaijan and Tajikistan) of total cephalosporin consumption and represented more than 50% of total cephalosporin consumption in nine of the 17 datasets (Fig. ES2).

Fig. ES2 Relative consumption of cephalosporins by generation

1 Kazakhstan data represent 80–85% of hospital and community sales.
2 North Macedonia data are community consumption only.

Consumption of Core Access agents dominated in all AMC Network countries and areas, representing between 46.4% (Georgia) and 72.3% (Bosnia and Herzegovina) of total antibacterial consumption in 2017.

Watch group agents represented between 22.9% (Bosnia and Herzegovina) and 44.4% (Tajikistan) of total consumption. Consumption of Reserve group agents was uniformly low across the Network (Fig. ES3).

Fig. ES3 Relative consumption of Watch group of antibiotics classes as a proportion of total consumption

4 Total consumption of antibiotics for this calculation includes J01, vancomycin (A07AA09), colistin (A07AA10), polymyxin B (A07AA05) and metronidazole (P01AB01).
5 Kazakhstan data represent 80–85% of hospital and community sales
6 North Macedonia data are community consumption only.

Changes to DDDs implemented in January 2019 impacted on both total and relative consumption estimates, driven mostly by DDD changes for several commonly used beta-lactam penicillins. Total J01 consumption estimates decreased from a range of 8.5–36.4 DIID using 2018 DDD values to 7.8–31.0 DIID
using 2019 DDD values. The percentage reductions in total DID ranged from 8.0% to 15.9%, with mean DID reductions of 12.7%. However, there was limited impact on rankings from highest to lowest total consumption in DID. The data from 2015 to 2017 with 2019 DDD values applied will provide new baseline trend data against which data for future years will be compared.

It was possible to examine consumption patterns in community and hospital settings separately in four cases (Kazakhstan, Montenegro, the Russian Federation and Turkey). Most consumption occurs in the community and choices of antibiotics differ considerably in the two settings. This is important information as interventions are developed to target problem prescribing practices with antibiotics.

**Discussion**

The report extends the analyses of data from the WHO Europe AMC Network from the 2017 report of the WHO Regional Office for Europe and a 2019 peer-reviewed manuscript (WHO Regional office for Europe, 2017; Robertson et al., 2019).

Notwithstanding the incomplete data capture in North Macedonia (community consumption only) and Kazakhstan (commercial data source captures 80–85% of hospital and community sales), the data in the report illustrate the large variability in reported consumption of J01 antibacterials across the AMC Network – ranging from 8.5 DID (Azerbaijan) to 36.4 DID (Turkey) in 2017. The mean consumption was 21.1 DID (median consumption 20.2 DID). These consumption estimates were mostly lower than those reported in 2011 (range 6.4 DID in Uzbekistan to 42.3 DID in Turkey, mean 23.6 DID) and in 2015 (range 8.0 DID for Azerbaijan to 41.5 DID for Turkey, mean 21.2 DID).

ESAC-Net analyses also show considerable variability in consumption estimates. In 2017, total consumption (hospital and community sectors combined) was available for 22 European Union/European Economic Area countries. Reported consumption ranged from 11.0 DID in the Netherlands to 34.1 DID in Spain (ECDC, 2018).

A notable change is the substantial reduction in consumption estimates for Turkey over time, which reflects sustained efforts at national level to improve antibiotics use. Turkish health authorities have implemented an electronic prescription system to track prescription data and provide feedback to physicians, and have adopted a rational drug use national action plan for 2014–2017 that prioritizes the appropriate use of antibiotics. Turkey estimates for 2011 (42.3 DID) relied on commercial IQVIA data and reflected community consumption; the comparable community estimate in 2015 was 40.1 DID, derived from the comprehensive pharmaceutical track and trace system that follows medicines from production to consumption. Data for 2017 were disaggregated to community and hospital consumption, with 35.2 DID in the community sector and 1.2 DID in the hospital sector. These 2017 data show the positive impacts of the sustained educational and regulatory interventions undertaken since 2014 in Turkey.

The extent of consumption of parenteral formulations also varied widely – 4% in Turkey and 5% in Bosnia and Herzegovina, up to 45% in Kyrgyzstan and 50% in Uzbekistan. The reasons for these substantial differences require investigation at national level. While there may be cultural and medical practice factors that favour injection use in some settings, oral medications have been shown to be associated with fewer complications, lower health-care costs and earlier hospital discharge without loss of clinical efficacy. There may be opportunities to work with clinicians and the public to reduce the use of injection formulations in some of the AMC Network countries and areas.

There was also considerable variation in the extent of consumption of the different pharmacological subgroups across the AMC Network. In 2017, cephalosporin (J01D) consumption varied from 9% to 27.5% of J01 consumption. Notably, third-generation cephalosporins (Watch agents) comprised more than
half of the total cephalosporin consumption in nine AMC Network countries. The individual chapters for each AMC Network country and area show the extent of use of agents like ceftriaxone. Given the limited indications for this agent, it could be useful to review existing guidelines and treatment protocols to check alignment with WHO Model List of Essential Medicines for adults recommendations (WHO, 2017c).

Quinolone (J01M) consumption varied across the network, with low levels of consumption in Uzbekistan and Kyrgyzstan up to 22.9% of total J01 consumption in Tajikistan.

Watch group agents (oral and parenteral formulations combined) represented between 22.9% and 44.4% of antibacterial consumption across the AMC Network. The relatively higher levels of consumption of specific Watch group antibiotics suggest some targets for further investigation, interventions and stewardship activities. Consumption of Reserve group agents was uniformly low across the Network.

Changes to DDDs implemented in January 2019 impacted on both total and relative consumption estimates, driven mostly by DDD changes for several commonly used beta-lactam penicillins. Total J01 consumption estimates decreased from a range of 8.5–36.4 DID using 2018 DDD values to 7.8–31.0 DID using 2019 DDD values. The percentage reductions in total DIDs ranged from 8.0% to 15.9%, with mean DID reductions of 12.7%, but there was limited impact on rankings from highest to lowest total consumption in DIDs. These decreases in total DIDs are a consequence of changes to measurement metrics rather than reflecting the results of any intervention by government, agencies or professional groups. Communication strategies will be required so stakeholders are aware of the impact of the DDD changes, along with re-setting of trend lines and targets for changes in antibiotic consumption at national level.

Data limitations must be acknowledged. The results presented are mostly based on import records and local manufacturer sales records. Importation records will be affected by the cycles of procurement and delivery, potentially giving rise to fluctuations in estimates of consumption that do not relate to actual use of antibacterials by patients and health-care facilities. Local manufacturer records need to be disaggregated to products for local consumption and products exported to other countries and areas.

The completeness, validity and reliability of the data should be considered when interpreting the results of the analyses. A fuller interpretation of the consumption data requires an understanding of the local context, taking account of changes in regulations (including enforcement of prescription-only status), data sources, resistance patterns and the potential impact of interventions to change practices.

The data presented summarize the experience to date of the WHO AMC Network. Despite some data limitations, the levels of consumption reported and, in some cases, the choices of antimicrobial agents used confirm the need for action. The variability between countries and areas suggests that differences in patterns of consumption are not solely related to differences in disease burden. The quantitative data on antibacterials in the report provide a starting-point for further studies to understand better the use of these medicines in clinical practice – this will require further quantitative and qualitative studies in primary care and hospital sectors.

Conclusions

The results presented in the WHO Regional Office for Europe Antimicrobial Medicines Consumption (AMC) Network: AMC data 2011–2017 report document trends in consumption of antibacterial agents across parts of non-European Union Europe. The notable feature is the wide variability of estimates (both volumes of consumption and selection of agents) across the WHO Europe AMC Network. While the quantitative metrics presented have limited application in assessing the appropriateness of prescribing, they illustrate differing patterns of antibiotic consumption over time and point to potential problems in antibiotic use.
The variability seen is unlikely to be explained by different patterns or burden of disease alone. The reasons for such variability require further investigation. The relatively higher levels of consumption of specific Watch group antibiotics suggest some targets for further investigation, interventions and stewardship activities supported by evidence-based guidelines and treatment algorithms.

A full exploration of reasons for the changes in consumption patterns reported in each of the 17 AMC Network countries and areas is beyond the scope of the report. However, the impact of locally produced antibiotics on treatment choices, pharmaceutical industry promotion, perverse incentives to prescribe and dispense antibiotics, and availability and use of up-to-date guidelines all need to be considered in developing interventions to improve antibiotic use.

References


* All weblinks accessed 1 April 2019.
The WHO Regional Office for Europe

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