Surveillance of antimicrobial resistance in Europe, 2021 data

Executive summary

WHO European Region

The results presented in this executive summary are based on antimicrobial resistance (AMR) data from invasive isolates reported to the Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR) network and the European Antimicrobial Resistance Surveillance Network (EARS-Net) in 2022 (data referring to 2021). In total, 16 countries reported data to CAESAR, while 29 countries, including all of those in the European Union (EU) and two from the European Economic Area (EEA) (Iceland and Norway), reported data to EARS-Net. While the EARS-Net and CAESAR networks use comparable methods for data collection and analysis, the results presented in this executive summary originate from distinct country surveillance systems. As these inherently are influenced by specific protocols and practices, caution is advised when comparing countries in terms of AMR patterns.

Epidemiology

The AMR situation in bacterial species reported to the AMR surveillance networks in 2021 varied widely depending on the bacterial species, antimicrobial group and geographical region. Resistance to third-generation cephalosporins and carbapenems was generally higher in *Klebsiella pneumoniae* than *Escherichia coli*. While carbapenem resistance remained rare in *E. coli* for most countries, 33% reported resistance percentages of 25% or higher in *K. pneumoniae*. Carbapenem resistance was also common in *Pseudomonas aeruginosa* and *Acinetobacter* species, and at a higher percentage than in *K. pneumoniae*. As observed in previous regional reports, there is a north-to-south and west-to-east gradient of resistance, with higher rates observed in the southern and eastern parts of the European Region. This was particularly evident for third-generation cephalosporin and carbapenem resistance in *K. pneumoniae* and carbapenem resistance in *Acinetobacter* spp.

Considering only the 13 countries that submitted data to CAESAR both in 2020 and 2021, the overall number of isolates reported was higher in 2021 than in 2020. This was a result of higher numbers of isolates being reported across all pathogens. These overall tendencies were not always observed at country level; however, all countries reported higher numbers of *Acinetobacter* spp. isolates in 2021 than in 2020. In all 16 countries submitting data to CAESAR in 2021, the majority of isolates (69.9%) were *E. coli* (38.0%), *Staphylococcus aureus* (17.1%) and *K. pneumoniae* (14.8%).

Looking at bacterial species-specific results in 2021, resistance to fluoroquinolones in *E. coli* was generally lowest in the northern parts of the WHO European Region and highest in the south. A resistance percentage below

10% was observed in two (4%) of 45 countries reporting data on this microorganism. A resistance percentage of 25% or above was reported in 17 (38%) countries. A resistance percentage of 50% or above was observed in four (9%) countries. For third-generation cephalosporin resistance in *E. coli*, 12 (27%) of 45 countries reported percentages below 10%, whereas resistance percentages equal to or above 50% were observed in four (9%). Eight (18%) of 44 countries reported carbapenem-resistant *E. coli* percentages of 1% or above.

Third-generation cephalosporin resistance in *K. pneumoniae* has become quite widespread in the WHO European Region. In 2021, percentages below 10% were observed in seven (16%) of 45 countries reporting data on this microorganism, while 19 (42%), particularly in the southern and eastern parts of the Region, reported resistance percentages of 50% or above. Carbapenem resistance was more frequently reported in *K. pneumoniae* than in *E. coli*. In 2021, resistance percentages were generally low in the northern and western parts of the WHO European Region; 14 (31%) of 45 countries reported resistance percentages below 1%. Fifteen (33%) countries reported percentages equal to or above 25%, eight of which (18% of 45 countries) reported resistance percentages equal to or above 50%.

Large differences were observed in the percentages of carbapenem-resistant *P. aeruginosa* in the European Region. In 2021, resistance percentages of below 5% were observed in two (5%) of 44 countries reporting data on this microorganism, whereas six (14%) countries reported percentages equal to or above 50%.

The percentages of carbapenem-resistant *Acinetobacter* spp. varied widely within the Region in 2021, from below 1% in three (7%) of 45 countries reporting data on this microorganism to equal to or above 50% in 25 (56%) countries, mostly in southern and eastern Europe.

In 2021, eleven (25%) of 44 countries reporting data on *S. aureus* had meticillin-resistant *S. aureus* (MRSA) percentages below 5%. MRSA percentages equal to or above 25% were found in 13 (30%) of 44 countries.

Large differences were observed across the Region in the percentage of penicillin non-wild-type *Streptococcus pneumoniae*. Two (5%) of 43 countries reporting data on this microorganism had percentages below 5% in 2021, whereas percentages equal to or above 25% were found in five (12%) countries.

Resistance to vancomycin in *Enterococcus faecium* varied substantially among countries in the Region. In 2021, resistance percentages of below 1% were reported by six (14%) of 44 countries reporting data on this microorganism, while percentages equal to or above 25% were found in 19 (43%), five of which (11% of 44 countries) reported resistance percentages equal to or above 50%.

Country-specific information for each bacterial species, including information on patient age group and sex, are available on the WHO European Region website [1].

Discussion

The results from CAESAR and EARS-Net clearly show that AMR is widespread in the WHO European Region. Although an assessment of the exact magnitude of AMR remains challenging, the presence of specific AMR patterns across clinical settings covered by the surveillance networks is apparent. High percentages of resistance to third-generation cephalosporins and carbapenems in *K. pneumoniae*, and high percentages of carbapenem-resistant *Acinetobacter* spp. in several countries are of concern. They suggest the dissemination of resistant clones in healthcare settings and indicate that many countries have serious limitations in treatment options for patients with infections caused by these pathogens. While the west-to-east gradient in AMR percentages is evident for gram-negative bacteria (*E. coli*, *K. pneumoniae*, *P. aeruginosa*, *Acinetobacter* spp.), it is less obvious for gram-positive bacteria (*S. aureus*, *S. pneumoniae*, *E. faecium*). As bacterial microorganisms resistant to antimicrobials cannot be contained within borders or regions, these results underline the need for concerted action to combat AMR throughout the WHO European Region, and globally.

The impact of the COVID-19 pandemic on AMR is apparent in many ways. Many countries providing AMR data to CAESAR reported more *E. coli* isolates in 2021 than in 2020. This may be related to a steady increase in healthcare activities in domains not linked directly to the COVID-19 response, possibly including more engagement in AMR surveillance activities. In addition, many countries in the WHO European Region reported higher numbers of *S. pneumoniae* isolates in 2021 than in 2020. This may be due to the increasing circulation of respiratory pathogens in the community post-lockdown and the removal of enforced measures to control the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). On the other hand, typical healthcare-associated pathogens such as *Acinetobacter* spp. and *E. faecium* were more frequently observed in many countries during 2021 than in previous years.

Overall, more countries and laboratories reported data to the European surveillance networks in 2021, which is an encouraging step in the right direction. Nevertheless, when looking at surveillance capacity in the WHO European Region: 16% of countries still reported that they only collected AMR data at local level and without a standardised approach. This highlights the ongoing need to strive for enhanced standardisation as systems and networks continue to grow and mature.

Since the publication of the Global Action Plan on Antimicrobial Resistance (GAP-AMR) in 2015 [2], most Member States of the WHO European Region have enhanced efforts to tackle AMR. In 2017, only 34 (68%) of the 50 countries reported having developed a national action plan (NAP) on AMR, but the latest round of global monitoring showed that this had increased to 44 (85%) of the 52 countries that responded in the Region. The challenge ahead is to ensure comprehensive implementation and adequate funding for NAPs.

Similarly, efforts to improve antimicrobial consumption in the Region remain heterogeneous. During 2021, 19 of 28 (68%) EU/EEA countries reporting data for both the community and the hospital sector met or exceeded the WHO country-level target of 60% of total antibacterial consumption being derived from WHO's Access category (as defined in the Access, Watch, Reserve (AWaRe)[1] classification list) [3]. Only five of 18 countries reporting to the WHO Regional Office for Europe Antimicrobial Medicines Consumption Network achieved this target in 2019 [4].

Public health implications

AMR is one of the top 10 global public health threats facing humanity [5]. Although the number of countries in the Region that heeded the global call [2, 6] to develop NAPs on AMR has reached a high level, and many countries are already embarking on a revision of their NAPs for the next phase of implementation, there are some countries that have only just begun to implement effective interventions to tackle AMR. The same applies to AMR surveillance. Greater efforts and investment are required to increase the comparability, quantity and quality of AMR surveillance data. Current patterns, such as increases in carbapenem-resistant *Acinetobacter* spp. isolates that are difficult to eradicate once endemic, underline the need to enhance efforts to prevent and detect resistance. These patterns also highlight the role AMR surveillance can play in strengthening health system resilience and preparedness.

There is still a lack of high-level support and robust funding for comprehensive programmes and interventions on infection prevention and control (IPC), antimicrobial stewardship and surveillance and it is clear that commitment from the highest-level of government is crucial to advance on the AMR agenda [7].

The COVID-19 pandemic has exposed the weaknesses in national health systems and the interconnectedness of countries and continents. The world is still adjusting to the effects of this pandemic on people and public health, and efforts to tackle AMR are only just beginning to find a balance after the repurposing of healthcare professionals to support the COVID-19 response throughout the European Region. Across the globe, governments were confronted with a need for more coordinated action and collaboration and this has paved the way for a more united front against future health threats, including AMR. It is hoped that such a united front will enable us to respond more effectively to the looming threat represented by AMR in the coming years.

This report highlights the persistent disparities in AMR prevalence across the WHO European Region and details unexploited opportunities for counteracting AMR.

1 AWaRe classifies antibiotics into three stewardship groups – Access, Watch and Reserve – to emphasise the importance of their optimal uses and potential for AMR.

EU/EEA countries

As in the preceding years, all EU Member States and two EEA countries (Iceland and Norway) reported data for 2021 to EARS-Net. All but one country reported data for all eight bacterial species under surveillance by EARS-Net (*E. coli*, *K. pneumoniae*, *P. aeruginosa*, *Acinetobacter* spp., *S. pneumoniae*, *S. aureus*, *E. faecalis* and *E. faecium*), while one country reported data for all bacterial species except *S. pneumoniae* [8].

Epidemiology

The most commonly reported bacterial species from EU/EEA countries in 2021 were *E. coli* (39.4%), followed by *S. aureus* (22.1%), *K. pneumoniae* (11.9%), *E. faecalis* (8.8%), *E. faecium* (6.2%), *P. aeruginosa* (6.1%), *Acinetobacter* spp. (3.0%) and *S. pneumoniae* (2.5%). *Acinetobacter* spp. had by far the largest annual increase in the number of reported isolates in both 2020 and 2021.

The reported AMR percentages for several bacterial species–antimicrobial group combinations varied widely among EU/EEA countries, often with a north-to-south and west-to-east gradient. In general, the lowest AMR percentages were reported by countries in the north of Europe and the highest by countries in the south and east of Europe.

Overall, for the EU/EEA (excluding the United Kingdom) and during the period 2017–2021, most of the bacterial species–antimicrobial combinations under EARS-Net surveillance showed either a significantly decreasing trend or no significant trend in the population-weighted mean AMR percentage. Exceptions included the increasing trends in the EU/EEA (excluding the United Kingdom) population-weighted percentage of aminoglycoside and combined resistance for *Acinetobacter* spp. (from 36.3% to 39.6% and 32.1% to 36.8% respectively), and the EU/EEA population-weighted percentage of carbapenem resistance for *E. coli*, *K. pneumoniae* and *Acinetobacter* spp. which increased from 0.1% to 0.2%, 8.1% to 11.7% and 37.6% to 39.9%, respectively. Reports of carbapenem resistance still remained relatively rare among *E. coli* isolates (0.2% in 2021). By contrast, in 2021, 11.7% of *K. pneumoniae* isolates and 39.9% of *Acinetobacter* spp. isolates were carbapenem-resistant.

In general, the EU/EEA population-weighted AMR percentages were lower in *E. coli* than in *K. pneumoniae*, *P. aeruginosa* and *Acinetobacter* spp. Nevertheless, 53.1% of all *E. coli* isolates reported in 2021 were resistant to at least one antimicrobial group under surveillance, compared to 43.0% of *Acinetobacter* spp., 34.3% of *K. pneumoniae* isolates and 18.7% of *P. aeruginosa* isolates. Among these four pathogens, combined resistance to several antimicrobial groups/agents remained a frequent occurrence: reported for 5.1% of *E. coli* isolates, 21.2% of *K. pneumoniae* isolates, 12.6% of *P. aeruginosa* isolates and 36.8% of *Acinetobacter* spp. isolates.

For *S. aureus*, a significant decrease in the EU/EEA (excluding the United Kingdom) population-weighted percentage of MRSA isolates was reported during 2017–2021, from 18.4% to 15.8%. Nevertheless, MRSA is still an important pathogen in the EU/EEA, with percentages remaining high in several countries.

For *S. pneumoniae*, the decrease in the number of cases observed in 2020 continued in 2021, both overall and for isolates resistant to the antimicrobials under surveillance.

The resistance profiles of both *Enterococcus* species under surveillance continue to be of concern. The percentage of *E. faecium* with vancomycin resistance continued to increase, reaching 17.2% in 2021. For *E. faecalis*, almost a third of all reported isolates had high-level resistance to gentamicin in 2021.

Country-specific information for each bacterial species, including results by patient age group and sex for specific AMR phenotypes, are available in ECDC's Surveillance Atlas of Infectious Diseases [9].

Discussion

In 2021, the AMR percentages for the bacterial species-antimicrobial group combinations under surveillance continued to be high overall in the EU/EEA. The increasing trends in carbapenem resistance for *K. pneumoniae* and *Acinetobacter* spp. and vancomycin-resistant *E. faecium* between 2017 and 2021 (when excluding the United Kingdom) are of particular concern and indicate that AMR remains a serious challenge in the EU/EEA. As in previous years, there was a large variability in the percentages across EU/EEA countries in 2021, highlighting the opportunities for significant AMR reduction through interventions to improve IPC and antimicrobial stewardship practices.

The data for 2020 and 2021 presented in this executive summary coincide with the first years of the coronavirus disease (COVID-19) pandemic. During 2020 and 2021, changes in human behaviour, resulting from efforts to control the pandemic, modified the risk of infection from pathogens with AMR [10-11]. Large decreases in the total consumption of antibacterials for systemic use (ATC group J01) were noted during the first two years of the pandemic, particularly in the community. However, changes were less consistent in the hospital sector, with increased consumption of last-line antibiotics such as carbapenems [3]. In 2020–2021, access to preventive, primary and elective healthcare, including surgery, was delayed. More specialised care (e.g. for late diagnoses) commonly requires interventions that predispose patients to a higher risk of infection from an antimicrobial-resistant pathogen, such as the use of antimicrobial agents and invasive devices [12]. In addition, admissions to Intensive Care Units (ICU) due to COVID-19 placed a strain on resources, which necessitated the re-purposing of non-ICU beds and the allocation of non-ICU staff to meet the urgent demand. In healthcare, as in society, recommendations were in place for conscientious IPC to protect against respiratory viral pathogens. However, compliance with all IPC measures in healthcare is likely to have been adversely affected by high hospital patient loads, staff absenteeism due to COVID-19, and reliance on more junior staff [13-15]. Nevertheless, EU/EEA countries have continued to strengthen their participation in EARS-Net. As a direct result, EARS-Net data can be used to confidently describe the ongoing AMR threat for the EU/EEA, since a majority of countries reported data that are nationally representative.

In 2022, ECDC used the national data reported to EARS-Net for 2016–2020 to estimate the burden of infections with antibiotic-resistant bacteria under surveillance in the EU/EEA [16]. Between 2016 and 2019, the number of cases increased from 685 433 to 865 767, before decreasing to 801 517 in the estimate for 2020. These infections resulted in an estimated annual number of attributable deaths that increased from 30 730 deaths in 2016 to 38 710 deaths in 2019, before decreasing slightly in 2020 to 35 813 deaths. In 2016–2020, the largest burden of disease was caused by infections with third-generation cephalosporin-resistant *E. coli*, followed by MRSA and third-generation cephalosporin-resistant *K. pneumoniae*. Infections with these three antibiotic-resistant bacteria resulted in the largest health impact, generating 58.2% of the total burden, measured in disability-adjusted life years (DALYs). ECDC estimated that for 2020, 30.9% of the total burden in DALYs was from infections with carbapenem-resistant bacteria. A similar number of deaths were attributable to carbapenem-resistant *K. pneumoniae*, (4 076 deaths), *Acinetobacter* spp. (3 656 deaths) and *P. aeruginosa* (3 210 deaths) [16].

For the period 2020 to 2021, the most worrying increase in the number of reported cases was for *Acinetobacter* spp., including isolates with carbapenem resistance. Although the reasons for the increased number of *Acinetobacter* spp. infections in many EU/EEA countries warrant further investigation, they are likely to be directly related to changes in healthcare provision due to the pandemic. Even hospitals that rigorously and conscientiously applied IPC practices may have experienced IPC breaches which would be sufficient for *Acinetobacter* spp. transmission [10].

Trends in *P. aeruginosa* cases might have been expected to follow those observed for *Acinetobacter* spp., given the rate of ventilator usage among hospitalised COVID-19 cases and the fact that it is also often linked to environmental sources, however these trends remained relatively unchanged.

The continued lower number of cases of *S. pneumoniae* may be related to reduced risk factors for such infections during the COVID-19 pandemic (e.g. a decrease in the frequency of inter-personal contacts, influenza incidence, and antibiotic prescriptions, and perhaps a lower incidence of blood cultures for community-acquired infections) [3, 17].

Public health implications

Despite the increased awareness of AMR as a threat to public health, the availability of evidence-based guidance for IPC, antimicrobial stewardship and adequate microbiological capacity, public health action to tackle AMR in the EU/EEA remains insufficient. Unless governments respond more robustly to the threat of AMR, it will become an increasing concern. Estimates based on data from EARS-Net show that in 2020, more than 800 000 infections occurred in the EU/EEA due to bacteria resistant to antibiotics, and that more than 35 000 people died as a direct consequence of these infections [16].

During the first two years of the COVID-19 pandemic (2020–2021), the most striking increase in the number of cases, compared to pre-2020, was for carbapenem-resistant *Acinetobacter* spp. infections, mostly in countries that had a relatively high percentage of carbapenem-resistant cases pre-pandemic. *Acinetobacter* spp., including carbapenem-resistant isolates, cause outbreaks and are difficult to eradicate once endemic. It is therefore likely that carbapenem-resistant *Acinetobacter* spp. will continue to expand in the EU/EEA in 2022. The options for outbreak preparedness, prevention and control described in ECDC's Rapid Risk Assessment 'Carbapenem-resistant *Acinetobacter baumannii* in healthcare settings – 8 December 2016', remain valid for hospitals and national authorities in EU/EEA countries [18-19].

Further investment in public health interventions is urgently needed to tackle AMR. This would have a significant positive impact on population health and future healthcare expenditure in the EU/EEA. It has been estimated that a mixed intervention package including enhanced hygiene, antibiotic stewardship programmes, mass media campaigns, and the use of rapid diagnostic tests would have the potential to prevent approximately 27 000 deaths each year in the EU/EEA. In addition to saving lives, such an intervention package could pay for itself within just one year and save around EUR 1.4 billion per year in the EU/EEA [20].

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Suggested citation: European Centre for Disease Prevention and Control and WHO Regional Office for Europe. Surveillance of antimicrobial resistance in Europe, 2021 data. Executive Summary. Stockholm: European Centre for Disease Prevention and Control; 2022.

ECDC ISBN 978-92-9498-593-4
TQ-05-22-384-EN-N
10.2900/85311

WHO ISBN 978-92-89058513