Expanding antimicrobial resistance surveillance in the WHO European Region: 10 years of the CAESAR Network
Acknowledgements

The CAESAR Network has been able to thrive due to the continued support from members of the WHO AMR working group, consultants, implementation partners and the donors who have funded the CAESAR network year after year. The long-term commitment to funding this tremendous effort across Europe and central Asia is deeply appreciated. Particular thanks go to the governments of Germany and the Netherlands, RIVM, as well as the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) for providing technical, financial and human resource support.

Abbreviations and acronyms

AMR    antimicrobial resistance
AST    antimicrobial susceptibility testing
CAESAR Central Asian and European Surveillance of Antimicrobial Resistance network
EARS-Net European Antimicrobial Resistance Surveillance Network
ECDC   European Centre for Disease Prevention and Control
EQA    external quality assessment
ESAC-Net European Surveillance of Antimicrobial Consumption Network
ESCMID European Society of Clinical Microbiology and Infectious Diseases
EUCAST European Committee on Antimicrobial Susceptibility Testing
GLASS Global AMR and Use Surveillance System
RIVM   Rijksinstituut voor Volksgezondheid en Milieu [Netherlands National Institute for Public Health and the Environment]
Celebrating 10 years of the CAESAR network

Surveillance is an important building block in the fight against antimicrobial resistance (AMR) (Fig. 1). Although 2022 marked 10 years of the Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR) network and the valuable work that members, partners and donors have undertaken to make it such a success, in many ways its work has only just begun. Robust investment in surveillance capacity and underlying health systems is urgently needed to create and sustain quality health and monitoring systems that are responsive to patient and public health needs.

Over the past ten years, the CAESAR Network has focused on including and engaging as many countries/areas as possible, to strengthen their capacities and capabilities to undertake effective AMR surveillance.

The CAESAR network has contributed to informing the public and policy-makers about the magnitude and the relevance of AMR for both individuals and health systems. Thanks to close collaboration with European Centre for Disease Prevention and Control (ECDC) and European Surveillance of Antimicrobial Resistance Network (EARS-Net), the CAESAR Network is contributing to harmonized AMR reporting across the WHO European Region. In combination, these two networks report surveillance data for almost all 53 Member States in the Region, thereby equipping decision-makers and those tackling AMR with better and more complete data than ever before.
Building a network for success

AMR surveillance has real-world implications: for patients; for quality of care in health systems; for a health workforce that is fit for purpose; for achieving universal health coverage; and, importantly, for national, regional and global health security. The data informs how antibiotics are prescribed and consumed and also informs strategies for responding to equity issues in countries/areas where there is a lack of access to antibiotics. With improved Region-wide data at hand, effective policies can be put in place to promote more responsible use of antibiotics and to identify and respond to new threats. The COVID-19 pandemic demonstrated how precarious health security is, and should be a powerful warning about the seriousness of AMR and implementation of measures to curb this.

The CAESAR surveillance approach

AMR knows no geographical boundaries. It travels across borders and continents with ease and threatens human health on a major scale.
In 2012 the WHO Regional Office for Europe and two key partners, the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the Rijksinstituut voor Volksgezondheid en Milieu [Netherlands National Institute for Public Health and the Environment] (RIVM) created the CAESAR Network, a subregional network of AMR surveillance systems intended to complete AMR surveillance for the entire WHO European Region; responding to key strategic priorities of the 2011 European strategic action plan on antibiotic resistance (1).

Since 2015 when the first CAESAR report covered 2014 data from five countries/areas, the network has expanded to 20 countries and one area (see Fig. 1), with 16 of these countries and one area now regularly submitting AMR data.

Sharing surveillance data is critically relevant and essential if AMR is to be kept firmly on the map and on the agenda of Member States.

Dr Hans Henri P. Kluge, Regional Director of the WHO Regional Office for Europe
[1] All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999)
In 2022 an important progressive step was taken when the Regional Office, alongside ECDC, for the first time first published an annual joint report entitled *Antimicrobial resistance surveillance in Europe* (2). Joint reports provide the most up-to-date information on AMR for the entire Region, with virtual maps available from the WHO AMR dashboard (3).

CAESAR network members continue to take part in capacity-building workshops tailored to their needs, monthly trouble-shooting clinics with subject matter experts and networking opportunities during the annual CAESAR network meeting. In addition, the network organizes annual external quality assessment exercises, allowing laboratories in the network to challenge themselves, benchmark their performance against others in the network and take corrective action. These experiences allow them to not only learn from experts in the field, but also to engage in peer-to-peer learning. Ensuring relevant information reaches as many people in the respective networks as possible is a challenge and virtual exchanges, in the form of clinics and webinars, go some way to rectifying this.

Beyond this, the CAESAR network encourages AMR focal points and network members to meet regularly to exchange practical experiences, knowledge, barriers and solutions – in order to strengthen their respective surveillance systems.

WHO engagement usually starts with nomination of a WHO AMR focal point, followed by a targeted assessment mission to identify strength and gaps of the current system. Tailored support for capacity-building is designed and continually reviewed.

One important principle of the network is to engage with each member according to their capacity. Targeted support is provided, through connecting members with opportunities, programmes and initiatives, to facilitate data reporting and continually improve the quality of the data. Through this tailored engagement several countries/areas have since started reporting AMR data internationally.
CAESAR and the Global AMR Surveillance System

The Global AMR and Use Surveillance System (GLASS) was initiated in 2015 by WHO in response to the adoption of the 2015 Global action plan on antimicrobial resistance (4). GLASS promotes a shift from surveillance approaches based solely on laboratory data to a system that includes epidemiological, clinical and population-level data. GLASS has been conceived to progressively incorporate data from surveillance of AMR in humans, such as monitoring of resistance and the use of antimicrobial medicines, including AMR in the food chain and in the environment.

GLASS is constantly evolving, but currently collects and reports data for the following pathogens and specimen types (Fig. 2). As of August 2022, 32 of 53 Member States of the WHO European Region are enrolled in GLASS.

**Fig. 2 CAESAR and GLASS pathogens**

<table>
<thead>
<tr>
<th>Selected pathogens for surveillance (covered by both CAESAR and GLASS)</th>
<th>GLASS also covers</th>
<th>CAESAR also covers</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Acinetobacter</em> spp.</td>
<td><em>N. meningitidis</em></td>
<td><em>Enterococcus faecalis (E. faecalis)</em></td>
</tr>
<tr>
<td><em>Escherichia coli</em> (E. coli)</td>
<td><em>H. influenzae</em></td>
<td><em>Enterococcus faecium (E. faecium)</em></td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em> (K. pneumoniae)</td>
<td><em>S. enterica serovar Typhi</em></td>
<td></td>
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<tr>
<td><em>Pseudomonas aeruginosa</em> (P. aeruginosa)</td>
<td><em>S. enterica serovar Paratyphi A</em></td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em> (S. aureus)</td>
<td></td>
<td><em>Shigella spp.</em></td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em> (S. pneumoniae)</td>
<td></td>
<td><em>N. gonorrhoeae</em></td>
</tr>
<tr>
<td><em>Salmonella</em> spp. (non-typhoidal)</td>
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</table>

**Sample types** | Blood, cerebrospinal fluid, urine, stool, sputum, swabs (urethral, cervical, rectal, pharyngeal) | Blood and cerebrospinal fluid only |
The CAESAR network has:

- created a new AMR surveillance platform of 20 countries and one area across the WHO European Region that promotes international standards, collects, collates and presents AMR data and supports members’ systems in their efforts to improve diagnostic accuracy by offering annual external quality assessments (EQAs) to more than 300 laboratories every year;

- identified key problem areas faced by some CAESAR countries/areas, as well as outside the Region, in building and strengthening their own AMR surveillance systems and ultimately their ability to address fundamental regional issues of health security;

- supported CAESAR countries/areas with targeted capacity-building according to their specific needs, whether this is at clinical, laboratory, university or government level. As a result, several countries and one area in the Region are now able to share AMR data internationally;

- improved methods and standards across many laboratories in CAESAR countries/areas, allowing quality AMR data to be collected and shared. Today 95% of the laboratories participating in the CAESAR EQA are using the European Committee on Antimicrobial Susceptibility Testing (EUCAST) standards for antimicrobial susceptibility testing (AST);

- encouraged a multidisciplinary approach through targeted projects supporting diagnostic stewardship in CAESAR countries and areas; and

- facilitated countries/areas to learn from each other’s experience and knowledge to improve AMR data collection and the development of surveillance systems. The network organizes annual network meetings and regular clinics and encourages that the network regularly engages and shares.

What has the CAESAR network accomplished in the past 10 years?

Member States can join GLASS by submitting an official expression of interest to the GLASS secretariat. For countries/areas that have officially joined GLASS, the WHO Regional Office for Europe coordinates data transfers for both CAESAR and EARS-Net to GLASS, to ensure that there is no duplication of reporting efforts.
The CAESAR Network is unique as it tries to cover all aspects of AMR. For example, if there are problems at the level of clinicians, we try to correct it by discussing clinical guidelines. If clinicians and laboratory specialists are not well trained, we address the root problem in the curriculum. During eight years of working with CAESAR I have seen dramatic changes in countries/areas as they are updating their scientific methods and today 95% of the laboratories participating in the CAESAR EQA are using the EUCAST standards for antimicrobial susceptibility testing. The level of discussion among members is far higher than previously, meaning the basic problems have been solved and we are now moving on to discuss more complex issues. Knowledge is being accumulated in the Network.

Networking is extremely important for any progress. Being able to learn what your peers are doing in other countries/areas, how theory translates in practice in different settings is indispensable experience. Surveillance goes hand in hand with good clinical and laboratory practice and increasing the quality of data for surveillance has huge impact on individual patient management as well. I feel privileged to be in a position to spread ESCMID views on education through interactive courses and to see many enthusiastic participants at courses in different countries/areas, eager to learn, eager to share their experience and improve their practice. I am proud to see the high quality of latest microbiological data provided by the CAESAR network, but am aware that there is still a long way to go before obtaining highly reliable surveillance data based on adequate sampling. But if you want to go far, never walk alone, this is what the networks are for!

Onur Karatuna, clinical microbiologist, ESCMID

Arjana Tambić-Andrašević, clinical microbiologist, ESCMID
When the CAESAR Network started in 2012, only five countries/areas submitted AMR data. In 2022, that number increased to 16 countries/areas, which is significant progress for the European Region. Many countries/areas did not have any data collection or management in place at all and now inspired by the activities of the CAESAR network, they have a starting point for a surveillance system. CAESAR has helped countries/areas to join an international network which gives institutions working to tackle AMR an elevated status within their countries/areas.

Jos Monen, CAESAR International Data Manager, RIVM

CAESAR is a network of networks, and that’s what makes it strong. A small initiative with just one laboratory involved can be the start. And then as more people and institutions get involved the messages we promote and the knowledge we broker through CAESAR continue to amplify. First within the country/area and then beyond. I enjoy the community of practice we have created with CAESAR and that it has become a fertile ground for innovation and for trying new approaches.

Saskia Nahrgang, Technical Officer AMR, WHO Regional Office for Europe

Honestly speaking, there have been huge changes in our country as a result of being part of the CAESAR Network. The most important change is a deeper appreciation and understanding within our medical community of the role of microbiology in routine clinical work. Clinicians have really started collaborating with our microbiologists and there is now greater trust than ever before in the hospitals that participated in the proof of principles study. Previously, microbiologists were isolated in the laboratory and there was no direct collaboration between them and the clinicians. For us, there was a breakthrough of barriers and it was a major step.

Kristina Gyurjyan, AMR Focal Point, Head of the Human Resource Management Department, Ministry of Health, Armenia
The role of the laboratory

The microbiology laboratory plays an important role in the surveillance, treatment, control and prevention of infections. Data generated by laboratories feed into surveillance systems and, therefore, laboratories’ ability to perform quality work and reliably test for resistance and identify microorganisms causing serious infections is critical.

More than 300 laboratories across all CAESAR countries/areas annually participate in the EQA (5). Typically, a package of six well-characterized bacterial strains is shared with surveillance network laboratories. The laboratories’ task is to correctly identify the strains and submit accurate antimicrobial susceptibility test results. It means laboratories can identify areas for improvement and it also allows for benchmarking across countries/areas and for partners to provide the right kind of targeted support. Many of the countries/areas now submitting data to CAESAR started by participating in the annual EQA exercise.
Laboratory strengthening

Laboratories are crucial in AMR surveillance systems. All over the world there are attempts at international standardization as to how AMR is detected, and through which methods. The CAESAR surveillance approach helps to standardize and therefore strengthen laboratory practices (Fig. 3). Laboratories in CAESAR countries/areas operate at different levels, some more developed than others, and many face serious challenges to their ability to meet these international standards. Lack of capacity, limited resources, and procurement and quality issues relating to equipment, diagnostics and materials hamper efforts.

Theoretical and practical training courses have taken place in laboratories to support them to implement the EUCAST standards and to correctly identify pathogens causing infection and their resistance patterns.

When countries/areas submit their AMR data, CAESAR partners (ESCMID, RIVM and WHO) work closely with the countries/areas to discuss both the quality of data and any issues faced in data collection. For those countries/areas providing high-quality representative data, a new initiative is providing support on how to make better use of data and help them to estimate the burden of AMR to feed into policy decisions.

A strong laboratory is a backbone to make any type of samples that enter the laboratory useful. If the laboratory cannot do a good job, there is no sense in collecting samples.

Onur Karatuna, clinical microbiologist, ESCMID
Fig. 3 The CAESAR surveillance approach
Using data for decision-making

AMR data have important implications for use by a range of health professionals and organizations; from clinicians to hospitals, to governments, to the private sector and to the United Nations. Accurate results from blood samples produced by a laboratory in a timely manner mean that clinicians can give patients appropriate and targeted care, which saves lives and improves health. Using the data prevents the emergence and spread of AMR in general, when clinicians choose the right antibiotic for the patient, which leads to a better health outcome and prescription of fewer antibiotics through less trial and error. Patterns of infection can help to identify poor hospital hygiene and support interventions to promote infection prevention and control in clinical settings. At the government level, data can show whether policies on AMR need to be developed, whether they are effective over time or not and support decision-making and planning to tackle AMR.

Routine sampling for AMR data: the proof-of-principle project

CAESAR collects data generated from routine clinical practice. The routine sampling of patients with bloodstream infections is a vital diagnostic step for the provision of appropriate clinical care, and the data generated can serve as a basis for national/area AMR surveillance.

We developed a five-year ‘National Action Plan to Tackle Antimicrobial Resistance in the Republic of Tajikistan 2018–2022’ that integrates human health, veterinary health and agriculture. In 2021 we revised the plan and included education, finance, economic development, water resources management, environmental protection and industry. The core objective of the plan is to establish a nationwide AMR surveillance system and has strategic activities to support this. However, the country does not yet have an effective data collection system and we need this to have clear information for decision-making.

Said Davlatzoda, Deputy Head of State Sanitary Epidemiology Surveillance Service, Ministry of Health and Social Protection of the Population, Tajikistan
To improve this situation, a proof-of-principle project took place in four countries: Armenia, Georgia, Tajikistan and Uzbekistan. In each country, three to five pilot sites participated. Sampling of patients meeting a set of pre-defined criteria was encouraged and diagnostic materials were provided by the project. In addition, interdisciplinary communication of caregivers was supported and training was held on all aspects of antimicrobial sampling and laboratory methods to perform susceptibility testing. As a result, each country achieved important insights into AMR levels and procedural issues in the diagnostic steps involved were uncovered. Clinicians realized the value of clinical microbiology as part of the diagnostic work-up of patients with suspected bloodstream infection. As a result, diagnostic tests were more frequently requested, which improved the laboratory routine in dealing with blood cultures and AST. Microbiologists were in turn able to provide more timely feedback of laboratory results to prescribers of antimicrobial drugs.

Eventually, these initial successes may allow for optimization of antimicrobial therapy and signify a start for a sentinel laboratory-based surveillance system for AMR.
What does the future hold for CAESAR?

The CAESAR Network will continue to grow from strength to strength. Focus has initially been on growing the network, both in adding more countries/areas and in enabling them to generate and share data, but also in the quantity and representativeness of data submitted annually. Looking to the future, it is clear that many CAESAR members need more intense and targeted support to strengthen their diagnostic stewardship, laboratories and data management systems. Many need to overcome supply and procurement challenges and the quantity and quality of data also needs to improve to enable the use of AMR data for national policy decisions. As countries/areas can learn from each other’s experiences, it is also vital for the CAESAR network to continue to perform the role of a collaborating platform to share lessons learned and practical advice. It is crucial for CAESAR to continue building professional multidisciplinary relationships and networks, both within and across countries/areas, and to collaborate closely with EARS-Net, keeping methodologies as closely harmonized as possible.

I hope that countries/areas will take ownership of the surveillance so they don’t see it as an obligation towards WHO, but rather as their tool to produce better data, and use it to guide their own interventions and improvement. They are increasingly connected to other countries/areas across the Region and can form part of a European-wide community of surveillance experts that share information and experience on equal terms.

Danilo Lo Fo Wong, Regional Advisor, AMR, WHO Regional Office for Europe
References


Additional reading


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The WHO Regional Office for Europe

The World Health Organization (WHO) is a specialized agency of the United Nations created in 1948 with the primary responsibility for international health matters and public health. The WHO Regional Office for Europe is one of six regional offices throughout the world, each with its own programme geared to the particular health conditions of the countries it serves.

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