Global Antimicrobial Resistance and Use Surveillance System (GLASS)

GLASS manual for antimicrobial resistance surveillance in common bacteria causing human infection

World Health Organization

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Abbreviations and acronyms

AMC	antimicrobial consumption
AMR	antimicrobial resistance
AST	antimicrobial susceptibility testing
ATC	Anatomical Therapeutic Chemical (classification system)
AWaRe	WHO Access, Watch and Reserve antibiotic categorization
CAESAR	Central Asian and European Surveillance of Antimicrobial Resistance
CFU	colony-forming units
CLSI	Clinical and Laboratory Standards Institute
EARS-Net	European Antimicrobial Resistance Surveillance Network
EGASP	Enhanced Gonococcal AMR Surveillance Programme
EQA	external quality assurance
FAO	Food and Agriculture Organization of the United Nations
GAP-AMR	Global Action Plan on Antimicrobial Resistance
GLASS	Global Antimicrobial Resistance and Use Surveillance System
IACG	(United Nations) Interagency Coordination Group on Antimicrobial Resistance
IQC	Internal quality control
MIC	minimum inhibitory concentration
NCC	national coordinating centre
NRL	national AMR reference laboratory
OIE	World Organisation for Animal Health
ReLAVRA	*Red Latinoamericana de Vigilancia de la Resistencia a los Antimicrobianos* (Latin American Network for Antimicrobial Resistance Surveillance)
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
UNEP	United Nations Environment Programme
WHO	World Health Organization
WHONET	Database software for the management and analysis of microbiology laboratory data developed by the World Health Organization

Introduction

1.1 Background

Antimicrobial resistance (AMR) is the presence of resistance to antimicrobial medicines in infectious agents such as bacteria, viruses, fungi and parasites. AMR poses a significant public health and economic threat to countries and different sectors across the 'One Health' spectrum. Especially alarming is the rapid global spread of bacteria and fungi that cause common infections and are resistant to multiple or all treatment options.

In May 2015, the Sixty-eighth World Health Assembly adopted the Global Action Plan on Antimicrobial Resistance (GAP-AMR) *(1)*. One of the five strategic objectives of GAP-AMR is to strengthen the evidence base through enhanced global surveillance and research. AMR surveillance is the cornerstone for assessing the burden of AMR and informing evidence-based action and local, national and global strategies.

The first Surveillance of antimicrobial resistance for local and global action consultation *(2)* was hosted by the Swedish Ministry of Health and Social Affairs and the Public Health Agency of Sweden in 2014. At this event, representatives from 30 World Health Organization (WHO) Member States from all WHO regions reaffirmed the need for a global human health surveillance programme to inform local, national and regional actions and to monitor the effectiveness of interventions. Participants provided input in the first version of the Global Antimicrobial Resistance Surveillance System (GLASS) manual for early Implementation *(3)*. They also agreed on a high-level road map for the further development of GLASS and suggested to review and, if necessary, revise the system after the initial five years of implementation. In October 2015, WHO launched GLASS to support the second objective of the GAP-AMR *(4)* and enrolment in countries, territories and areas[1] began in 2016.

1.2 GLASS early implementation and revision

GLASS early implementation covered the period 2016–2022. The key objectives of this phase have been to launch the global surveillance system and provide guidance and technical support to countries to develop the foundation of national AMR surveillance systems.

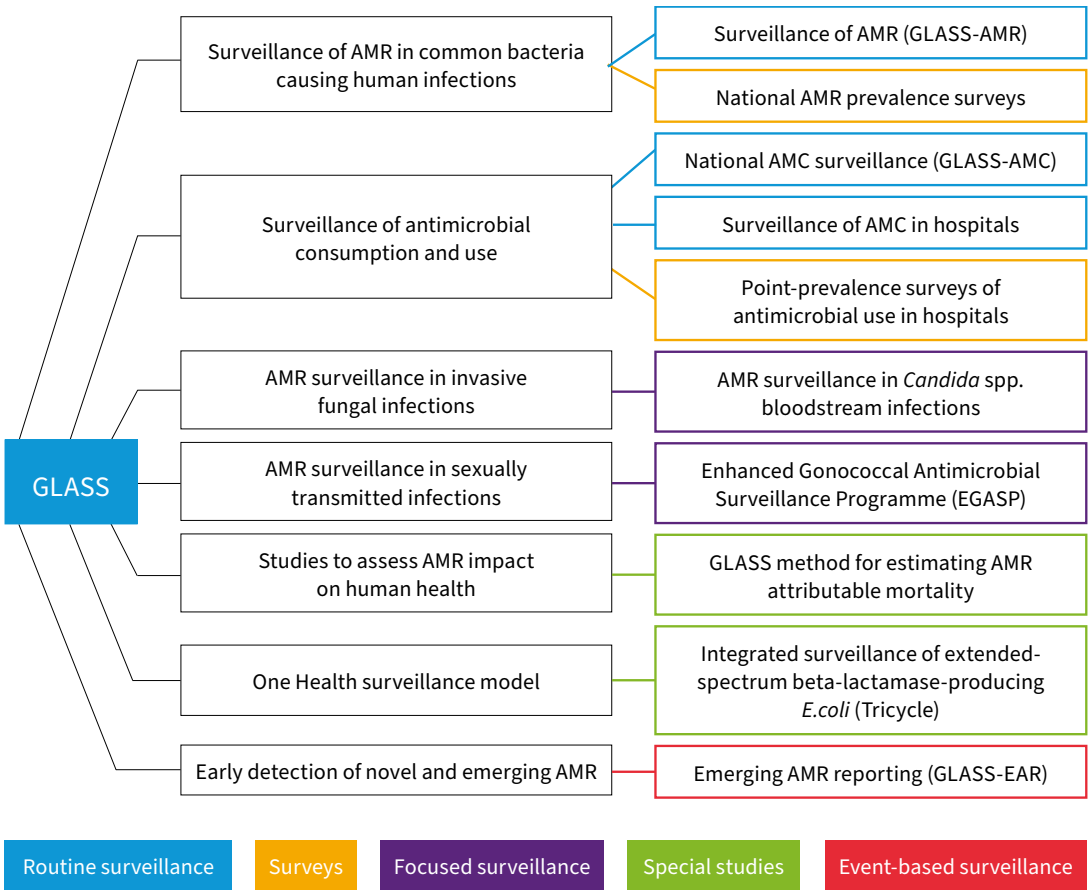
During the early implementation period, GLASS provided a standardized approach for the collection, analysis and sharing of AMR data by countries. It also sought to monitor the implementation status of existing or newly developed national AMR surveillance systems. GLASS has promoted a shift from surveillance approaches based solely on laboratory data to a system that also includes epidemiological, clinical and population-level data. In this first phase, GLASS has provided standards and tools for routine surveillance based on microbiological, epidemiological and clinical information on priority bacterial infections in humans. Country enrolment began in 2016. To date, GLASS has produced five global reports *(5–9)* on national surveillance systems' implementation progress and AMR surveillance data.

GLASS was designed to evolve continuously, starting with AMR surveillance based on clinical specimens sent routinely to laboratories for diagnostic purposes, followed by new components covering different types of surveillance activities (Fig. 1.1). A major step forward was the addition in 2019 of the global surveillance of antimicrobial consumption (AMC) in the human population [2] to be reported on an annual basis. Another important development was introduction of a "two-pronged" approach for AMR surveillance which involves both continuing data collection based on routinely available data ("routine surveillance") and application of complementary strategies such as national prevalence surveys to improve quality, completeness, and representativeness of data.

1 Any further reference to "country" and "national" in this publication should be understood to refer countries, territories and areas as well as national and local institutions, data and information. Use of the terms "country" and "national" does not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities.

2 The OIE, supported by the FAO and WHO within a quadripartite collaboration, has taken the lead to build a global database on antimicrobial agents intended for use in animals (https://www.woah.org/en/document/annual-report-on-antimicrobial-agents-intended-for-use-in-animals/).

Fig. 1.1. GLASS activities



In addition, event-based and focused AMR surveillance and special surveillance studies have been developed which are currently in different phases of implementation.

The GLASS Emerging Antimicrobial Resistance Reporting (GLASS-EAR) component *(10)* is an event-based surveillance component of GLASS to promote the early identification, management, and reporting of emerging AMR. Focused surveillance activities include the Enhanced Gonococcal Antimicrobial Surveillance Programme (EGASP, a collaboration between WHO and the United States Centers for Disease Control and Prevention) *(11)*, and the surveillance of AMR in bloodstream infections caused by Candida spp. *(12)*.

In alignment with the GAP-AMR 'One Health' principles, GLASS also promotes integration with other surveillance programmes with a relevance to human health, including the animal and plant production and environment sectors *(13)*. It contributes to the efforts by the quadripartite collaboration that includes the Food and Agriculture Organization of the United Nations (FAO), the World Organisation for Animal Health (OIE), the United Nations Environment Programme (UNEP) and WHO. The GLASS 'One Health' AMR surveillance model proposes assessing the occurrence of extended-spectrum beta-lactamase-producing *Escherichia coli* (ESBL-E.coli) across the human, environmental and animal sectors (named the "Tricycle" project) *(14)* and this is already applied in several countries. Application of the GLASS methodology for estimating attributable mortality due to selected types of AMR *(15)* has also begun in a few countries.

Hence, the original GLASS structure has evolved during the early implementation phase into a much broader system of normative guidance and tools including AMC, focused surveillance, national surveys, event-based surveillance and study protocols. This evolution should be seen in the context of different country needs and capacities, emerging AMR, and WHO's ambition to develop the evidence base to obtain reliable and representative data to develop national and global AMR burden estimates and inform the AMR response. However, revising GLASS is not just about adding activities, but also about recognizing that many countries cannot yet produce reliable and representative surveillance data.

The GLASS revision took into consideration the lessons learned from GLASS early implementation, its current limitations and challenges, as well as suggestions and proposals for further development made by participating countries, WHO regional and country offices, and international partners. GLASS development and revision have been supported by the WHO AMR Surveillance and Quality Assessment Collaborating Centres Network *(16,17)*. The revision is based on formal and informal input from GLASS national focal points and implementing partners, assessment missions, special initiatives such as Northern GLASS *(18)*, feedback from

the United Nations Interagency Coordination Group on Antimicrobial Resistance (IACG) working paper on surveillance and monitoring for antimicrobial use and resistance *(19)*, the AMR Strategic and Technical Advisory Group *(20)* and published scientific papers *(21–29)*. The current version of this manual has also been informed by the feedback systematically collected for the 3rd High level technical consultation and meeting on surveillance of antimicrobial resistance and use for concerted actions in April 2021[3], co-sponsored by the Republic of Korea and Sweden. Delegates from 88 countries, technical experts, stakeholders, and representatives from the WHO, FAO and OIE discussed methodological steps to improve the quality, robustness, and representativeness of data generated through GLASS, and strategies for strengthening and expanding GLASS to accurately inform the response to AMR at local, national, regional, and global levels.

1.3 Scope and purpose of the manual

This manual provides an update of the GLASS methods for AMR surveillance, superseding the 2015 GLASS manual *(3)*. It is part of a package of documents and tools designed to inform GLASS implementation and describes the objectives and methodology of GLASS-AMR, the GLASS component dealing with the global surveillance of AMR in selected bacteria causing common human infections. It is important to note that this manual does not cover the other GLASS activities shown in Fig. 1.1.

The purpose of this manual is to provide guidance for countries on the methods and metrics for the surveillance of AMR in selected bacteria causing common human infections. The development and implementation of AMR surveillance at national and local levels are addressed in more depth in a companion document *(30)*.

The intended readership of the manual includes national GLASS focal points, national public health professionals and health authorities responsible for AMR surveillance in humans, and those contributing to national surveillance data collection. It may also be helpful for national professionals from other sectors supporting surveillance of AMR in the context of the 'One Health' approach.

1.4 What is new in GLASS methods for AMR surveillance?

While the AMR surveillance metrics have not been dramatically changed in the current revision, several modifications and additions have been made, including the following:

- an approach to assessing and improving the validity and representativeness of routine surveillance data has been introduced to guide the interpretation of the data reported by countries and monitor the development of the national surveillance systems and their quality;
- introduction of periodic nationally-representative prevalence surveys *(31)* to complement and inform further development of routine surveillance to improve the quality and representativeness of data;
- an option for submission of anonymized, individual, patient-level data has been included, providing opportunities for improving AMR surveillance data analysis and enhancing its utility for decision-making;
- cerebrospinal fluid (CSF), respiratory samples, and two additional specimen types (rectal and pharyngeal swabs) for the surveillance of AMR in gonococci have been added to the GLASS list of specimens;
- five new pathogens have been added, including *Pseudomonas aeruginosa, Neisseria meningitidis, Haemophilus influenzae, Salmonella enterica serovar Typhi, and Salmonella* enterica serovar Paratyphi A;
- several antimicrobials have been included to describe the resistance of newly added target pathogens and to include both first- and second-line antimicrobials according to the WHO Access, Watch and Reserve (AWaRe) antibiotic categorization *(32)*;
- an option for submission of data generated by molecular AMR diagnostics has been included to complement phenotypic AMR diagnostics data and improve understanding of the underlying mechanisms responsible for resistance.

In the coming years, GLASS will further expand the global surveillance of AMR to secure better quality, more robust and more representative and accurate data. In addition to continuing to gather AMR data based on routine clinical patient sampling ("routine" surveillance), GLASS will also promote and assist the application of national AMR prevalence surveys to help accelerate the generation of accurate and representative quality data to inform national, regional and global actions. This two-pronged approach will permit a comparison of AMR patterns over time and between countries and generate reliable measures of the magnitude of the AMR.

3 https://www.who.int/news-room/articles-detail/3rd-member-states-technical-consultation-on-surveillance-of-amr

2 Objectives of GLASS AMR surveillance

GLASS will continue to collect, analyse and report harmonized data on AMR in infected patients at the national level, following the standards described in this manual.

The objectives of GLASS AMR surveillance in common bacteria causing human infections are to:

- generate data to inform AMR prevention and control strategies and assess the impact of interventions;
- foster national AMR surveillance systems and harmonize global standards;
- monitor global AMR trends in bacteria causing common infections in humans and inform the *WHO Model Lists of Essential Medicines (33)*;
- estimate the extent and burden of AMR globally by selected indicators;
- detect emerging resistance and its international spread; and
- inform research and development of new tools for the prevention, diagnosis and treatment of human infections caused by common bacterial pathogens.

3 Core components of a national AMR surveillance system

GLASS will continue supporting Member States in implementing national surveillance of AMR and collecting official AMR data through national focal points designated by ministries of health or national public health institutions responsible for national AMR surveillance. The functions and steps to establish or strengthen the core components of national surveillance systems are described in more detail elsewhere *(30)*. The core components include a national coordinating centre (NCC), a national reference laboratory (NRL), and surveillance sites. A brief description is provided below.

3.1 National coordinating centre

The national authorities designate the institution to undertake the NCC function. This institution should be experienced in conducting and managing national surveillance and have epidemiological expertise as well as access to clinical and microbiological expertise whenever needed. The NCC oversees the national AMR surveillance programme, gathers national AMR data, and ensures the system is functional. The NCC's roles should include:

- defining national AMR surveillance objectives within the national AMR action plan;
- defining the national AMR surveillance strategy and related indicators to achieve national or sub-national representative quality data;
- preparing and coordinating the dissemination of national protocols;
- coordinating data collection, analysis and reporting;
- sharing national data with WHO (GLASS).

A national focal point is identified at the outset and serves as the central point of contact within the NCC for all parts of the national AMR surveillance system and GLASS. The NCC should continuously monitor and evaluate the national AMR surveillance system. The national coordination function is usually undertaken by a public health institution or a government (ministry of health) department. It must have access to epidemiological and statistical expertise and appropriate capacities, work alongside the NRL for microbiology expertise, and have a defined structure for surveillance coordination and data management. The NCC should define a strategy for the implementation of surveillance standards and gradual expansion of the network to include all geographical areas and lower levels of the health system in order to achieve national or subnational representativeness. It should promote links between AMR surveillance in humans, food, animal and plant production, as well as the environment, with the ultimate aim to ensure coordination for AMR surveillance across these sectors. In addition, NCC activities include developing and maintaining functional links with AMR surveillance in other sectors, as well as with surveillance of AMC and antimicrobial use.

3.2 National reference laboratory

Upon enrolment in GLASS, countries are requested to designate at least one NRL [4] with expertise in methods for characterizing AMR pathogens. The NRL provides support to the national AMR surveillance system and promotes and facilitates good laboratory practice in the country, including the harmonization of methods and standards used in the national AMR surveillance system *(34)*. It oversees antimicrobial susceptibility testing (AST) methods and quality performance of the laboratories supporting surveillance sites participating in the national AMR surveillance, and investigates unusual or anomalous resistance patterns before they are reported to the relevant national authority. The NRL has a key role in the confirmation and reporting of emerging resistance in accordance with the GLASS-EAR reporting framework *(35)*. The NRL should work alongside the NCC in standardizing and verifying microbiological results. If the capacity to fulfil NRL tasks is not yet available within a country, collaboration can be temporarily established with another appropriate institute within or outside the country. To this effect, the WHO AMR Surveillance and Quality Assessment Collaborating Centres Network *(17)* has been established to assist WHO in supporting Member States to build the capacity to develop and implement AMR surveillance, particularly in low- and lower-middle income countries. The Network can also assist NRLs with confirmatory testing and further characterization if necessary.

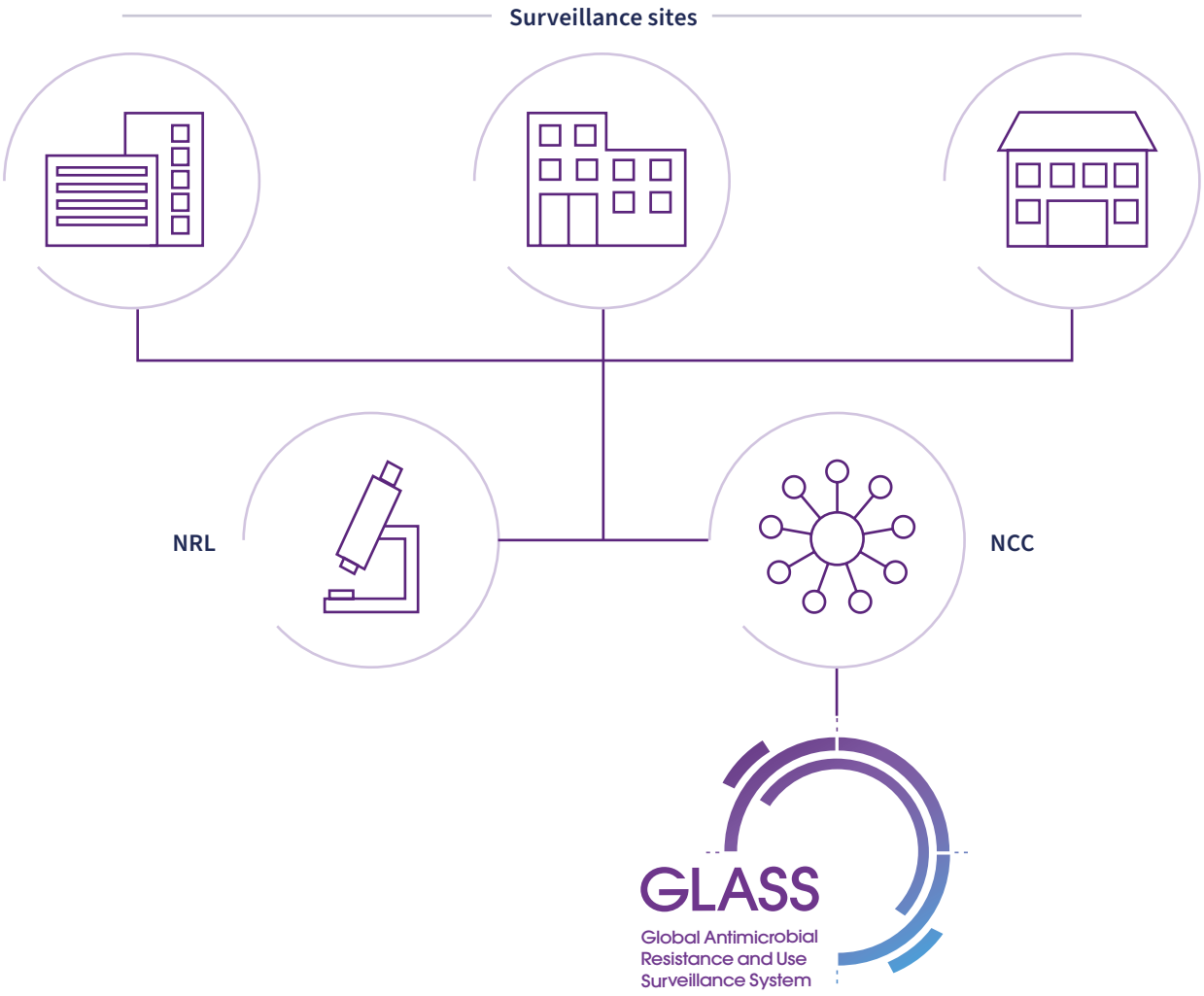
4 Some countries prefer having a network of several reference laboratories covering specific pathogens

3.3 Surveillance sites

The surveillance sites are the foundation of the surveillance system. The quality of data generated by the surveillance system is dependent on well-functioning surveillance sites capable of identifying and sampling patients with suspected infections, collecting clinical and epidemiological patient information, performing appropriate microbiological testing, and providing a timely reporting of results. Surveillance sites for AMR in humans are usually primary, secondary or tertiary care hospitals, or outpatient clinics with staff with clinical expertise to properly identify patients with infections, with access to quality-assured bacteriology laboratory support and appropriate data management systems to report basic clinical, epidemiological and microbiological data from patients included in the surveillance system *(36)*. The selection of participating sites depends on the country population distribution, and feasibility considerations, while aiming for a sustainable population coverage that is as representative as possible *(37)*. Participating countries are expected to implement a surveillance strategy to achieve high quality and representative surveillance data with balanced geographical, demographic and socio-economic sample characteristics. The selection of both inpatient and outpatient health care facilities is important for achieving a representative patient mix. The inclusion of specialty clinics may be considered for some targeted types of AMR, such as sexually-transmitted infection clinics for AMR gonorrhoea surveillance. In most LIMCs the number and types of reporting sites will gradually expand over time as the result of overall health systems strengthening. This may affect AMR rates and should be taken into consideration when interpreting AMR trends using routine surveillance.

These core components link together through a constant flow of data and information exchange, building an effective network for the detection and monitoring of infections and AMR. The flow of information linking surveillance sites with the NRL and NCC should be aligned with existing national health information systems to sustain data management processes and to integrate AMR data with other health data.

Fig. 3.1. GLASS core components



4 AMR surveillance principles

A surveillance system that is representative reflects the population characteristics related to time, place and person. Thus, it accurately observes both the occurrence of the health event over time and the distribution by person and place of that event in the population at any point in time. Two main factors need to be considered by countries when implementing AMR surveillance.

1. **System capacity for generating results that represent the true proportion of AMR in a defined population.** When investigating a condition in a population, the theoretical approach is to survey all the individuals within that population. For obvious reasons, this is very costly, time consuming, logistically demanding and almost impossible to implement in large populations. The number of sites will depend on the country and no single algorithm applies for determining the appropriate number. Participating countries are expected to establish at least one surveillance site and then extend the number progressively, aiming for a balanced geographical, demographic and socioeconomic distribution. Statistical methods can help to identify a sample of individuals that is representative of the whole target population, so that the outcomes generated reflect the occurrence in the larger entity and thus help countries in their strategy to progressively expand the surveillance network.
2. **System capacity to capture all symptomatic patients constituting the defined population for which AMR rates are estimated.** Even when a clear case definition is available for a specific syndrome, clinicians do not always take samples for microbiological culture and AST from all patients with suspected infection. Clinicians might only take samples from certain patients based on observed symptoms or risk factors, clinical perception, cultural belief or available resources. Such differences in individual clinical practice can lead to biased estimates of AMR occurrence as diagnostic results — both bacterial identification and AST — might not be available for all patients with suspected infection.

Countries have several options to help control existing constraints: they can put policies in place that secure access to health care to all in the need; provide adequate microbiology laboratory capacity; adequately set up surveillance system core components that can assure effective governance, coordination and monitoring; and strengthen patient care and appropriate AMR diagnostic stewardship to the best possible extent. Finally, countries can apply methods to assess current surveillance systems to help control selection biases and gauge the quality of the generated information.

The early implementation phase of GLASS and the findings of the 2022 GLASS report show that many countries, especially low- and middle-income countries, need to increase the coverage, representativeness and quality assurance of laboratory testing to be able to adhere to the abovementioned principles.

In this context, WHO should work towards the development of several strategic approaches to help countries to strengthen routine surveillance and implement combined epidemiological approaches (for example, surveillance and repeated surveys).

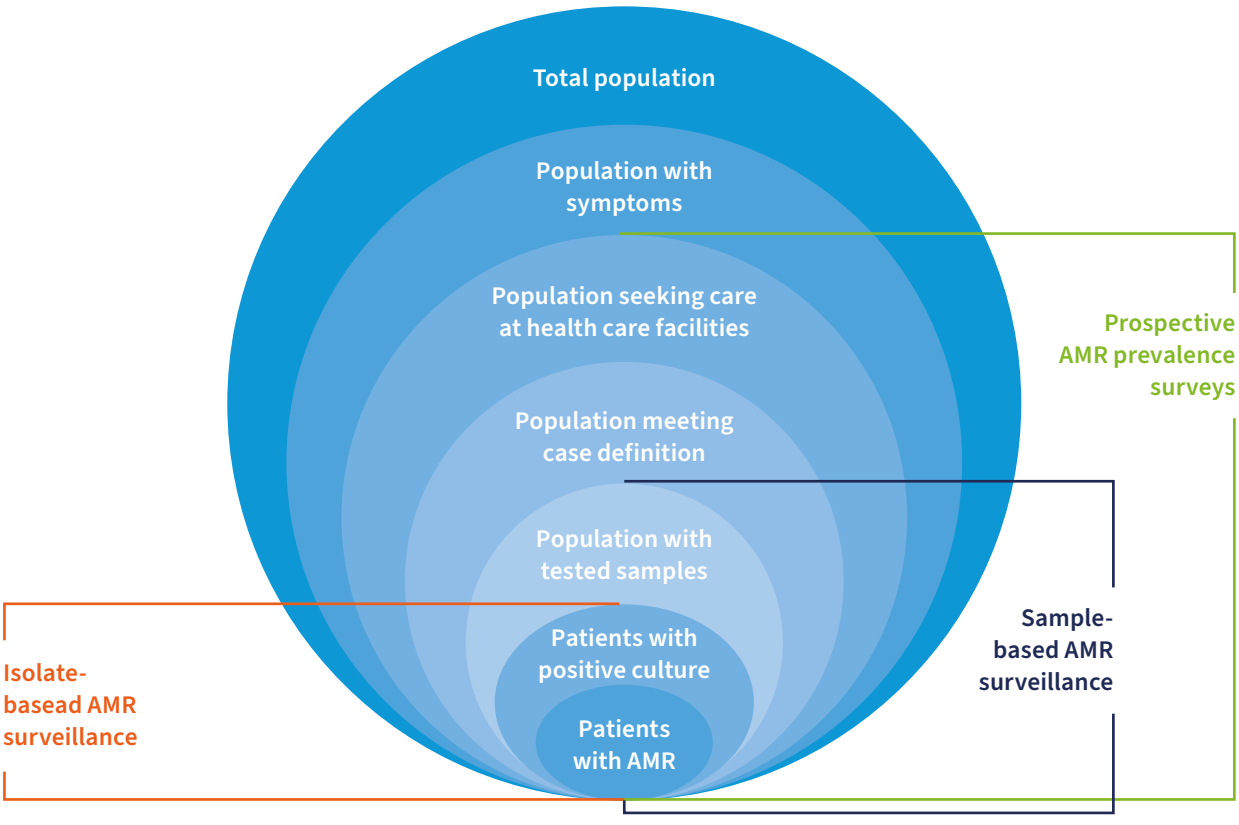
5 GLASS approaches for AMR surveillance

5.1 Population under surveillance

The population under surveillance is composed of patients seeking care in healthcare facilities with symptoms suggestive of infection. According to the type of approach, either routine surveillance (GLASS-AMR) or prevalence surveys (GLASS-AMR surveys), the population under study is illustrated in Fig. 5.1 and described below.

- **GLASS-AMR:** In the surveillance based on routine clinical patient testing (referred to as "routine" AMR surveillance), the population under surveillance includes all patients for whom clinical samples are collected for routine microbiological investigations, including species identification and AST.
- **GLASS-AMR surveys:** In the AMR prevalence survey, the population under survey includes all patients seeking care at health care facilities who meet the infection case definition and for whom clinical samples are collected for quality-assured microbiological investigations, including species identification and AST.

Fig. 5.1. Patient populations in "routine" AMR surveillance (isolate-based and sample-based surveillance) and prevalence survey approaches



5.1.1 Considerations when targeting the population of patients seeking care

The method described in this document generates AMR estimates for the subset of the national population that seeks and has access to health care and laboratory tests. However, self-treatment at home or treatment at a local pharmacy or drug dispenser can be very frequent in certain settings and be a driver for AMR. Thus, additional studies must be designed and run in parallel to estimate AMR in the proportion of the population that cannot be captured by health care facility-based approaches. Community-based surveys, health care facility access behaviour surveys and patient-pathway analyses can help to fill this gap with essential information *(40)*.

5.2 Data collection

GLASS requires AMR data to be collected through a surveillance system that gathers results from susceptibility testing for priority human bacterial pathogens isolated from clinical specimens sent to laboratories for diagnostic purposes. Together with patients' microbiological results (species identification and AST), countries are also asked to report a few clinical, demographic and epidemiological variables (Section 8), either in aggregated (Section 8.1) or individual-level format (Section 8.2).

5.2.1 Routine AMR surveillance

For the purpose of this manual, the following terminology will be used to refer to the two types of AMR surveillance data currently collected by GLASS-AMR routine surveillance approach:

- **Isolate-based** data include information on the patient population with laboratory confirmed infections caused by the defined target pathogens under surveillance (Fig. 5.1). They provide information on the proportion of patients with positive samples whose infections are caused by target pathogens resistant to specific antimicrobials (see Section 10.1).
- **Sample-based** data include information on the whole patient population with suspected infection from whom the clinical specimens have been collected (Fig. 5.1). This population comprises patients with laboratory-confirmed infection caused by the target pathogens, as well as patients with no microbial growth in collected specimens and those with positive samples with the growth of any other organisms, including other pathogens and commensal organisms. The sample-based approach allows to calculate the frequency of infections caused by different pathogens as well as antimicrobial-resistant pathogens in the patient population under surveillance (see Section 10.1).

Isolate-based data is a subset of sample-based data (Fig. 5.1). In both isolate-based and sample-based approaches, the patient population covered includes only those with a specific syndrome that seek care at a health care facility and from whom the clinical specimens have been collected based on routine local diagnostic practices. As diagnostic stewardship and access varies significantly, not all patients meeting certain clinical criteria may be included under routine conditions.

Although both isolate- and sample-based data can be reported to GLASS, WHO encourages countries to collect and report sample-based data. Isolate-based surveillance only provides data on resistance patterns within the bacterial population as the information is only collected for patients infected by pathogens under surveillance. Sample-based surveillance can provide insight into the frequency of infection and resistance patterns in the population undergoing testing according to specimen types. In settings where patients with suspected infections are systematically tested, the sample-based approach provides a proxy for all patients with the infection under surveillance. For example, using the tested population as the denominator allows an estimation of the frequency of reported infectious syndromes, the rate of positive culture and pathogen identification, associated or not with AMR. This can be stratified to identify the prevalence of AMR by demographic or epidemiological categories, for example by age, gender, hospital or community infection onset.

5.2.2 AMR surveys

The variables collected for the national AMR prevalence surveys are the same as for the GLASS-AMR routine surveillance approach as described in the "Individual-level dataset" (Sections 8.2.1 and 8.2.2). The difference resides in the fact that cases are prospectively and actively identified, using standardized case-definitions, and the selection of surveillance sites (health care facilities) is prospectively defined to achieve national representativeness and data accuracy. The implementation of AMR prevalence surveys is a controlled activity that is closely monitored and uses WHO-approved protocols and standardized methods, including international laboratory standards. Surveys can become invalid if the methods are not adhered to.

A comparison of types of data collected in routine AMR surveillance (isolate-based and sample-based surveillance) and in AMR surveys is shown in Table 5.1.

Table 5.1. Types of data collected in the surveillance approaches

Type of data collected	AMR surveillance data		
	Routine surveillance		AMR prevalence surveys
	Isolate-based	Sample-based	
Information from patients with AST results for bacterial pathogens and antibiotics under surveillance.	•	•	•
Information from patients from whom samples have been collected for microbiological testing (both with and without growth of the bacterial pathogens under surveillance).		•	•
Information from patients seeking care at the health care facility who meet the case definition of the infection under surveillance (both with and without growth of the bacterial pathogens under surveillance).			•

5.3 Considerations when generating AMR estimates for the target population using data collected through the surveillance system

In any surveillance system, the data collected and reported often represent only the tip of the iceberg, frequently because of biases associated with the system design. In the case of AMR data, selection bias is one of greatest concern *(38)*. Selection bias leads to a distortion in the estimate of the effect (that is, the frequency of isolates of a pathogen that are resistant to an antimicrobial agent), resulting from the way subjects (or isolates) are selected from the study population. For instance, data are often collected from a convenient subset of health care facilities located in defined geographical areas (for example, main cities), or representing a selected type of care (for example, tertiary hospitals). In addition, patients in wards dedicated to certain medical specialities or the more critically ill might be more likely to be sampled for infection caused by resistant bacteria (for example, intensive care units or surgical wards) *(39)*. However, it should be noted that the bias does not exactly come from the data directly, but rather in the generalizations, interpretations, and applications drawn from the data. If the data are collected predominantly from city hospitals for example, the national overview would not be complete, but the data can be representative of city hospitals. The error would be made if the estimates from the city hospitals are used to inform treatment guidelines for rural communities.

If a surveillance system reports on nearly all occurrences of a health event for the target population, then the system is by definition representative *(40)*. By contrast, if it is known that the health care service coverage of the target population is not comprehensive, selection bias might cause the surveillance system to generate data that will over- or underestimate the true frequency of AMR in the target population and the obtained AMR rates will not be representative.

When capacity is in place, probability sampling methods used for designing national surveys *(31)*, may be used to guide the design of surveillance systems to improve representativeness. This sampling approach helps to select facilities from the national list to optimize the representation of the target population in the sample.

Prospective AMR prevalence surveys address patient selection and testing biases as all patients seeking care in a health care facility and who meet the clinical definition of a given infectious syndrome are systematically tested using international laboratory norms and standards. While this represents a significant advantage over routine surveillance, this approach does not address the gap of the patient population that does not seek or reach a health care facility.

5.4 Assumptions and limitations of GLASS-AMR surveillance based on routine clinical patient sampling

There is no perfect surveillance system. Nevertheless, this does not disregard the importance and value of the information collected and reported. It is essential to identify and understand the limitations of the system and to take into account several considerations when interpreting the data generated following the GLASS-AMR routine surveillance approach.

Both isolate- and sample-based approaches are dependent on the following assumptions.

1. That patients with a specific syndrome who seek care at a health care facility will be assessed by a health care professional and sampled according to best clinical practice. The sample will then be properly transported to and processed by a quality-assured clinical laboratory for diagnostic microbiology investigations including culture and AST.
2. That the growth of a pathogen in selected specimens is a proxy for patient infection in the associated anatomical sites (for example, bloodstream infection, urinary tract infection, lower respiratory tract infection, enteric infection, urogenital infection). For this to be true, submitted microbiological data must relate to a true episode of illness in a patient, which is dependent on the diagnostic criteria locally applied.
3. That the number of isolates with AST results can be used as a representation of the number of patients infected with the targeted susceptible or resistant bacteria in a specific anatomical site, after removal of repeated isolates of the same pathogen from the same specimen type from the same patient (see Section 9.5.1).

Although there are several limitations linked to these assumptions, they form the foundation for AMR surveillance based on routine patient sampling. Understanding the sources of bias and eventual flaws generated by each assumption is essential to interpret generated data, and to address the need for the implementation of additional surveillance approaches.

5.4.1 Limitations of routine diagnostic results for surveillance purposes

Some of the main limitations of AMR surveillance based on routine clinical practices are listed below and can be more prominent in countries with limited resources.

1. Lack of, or limited access to health care and a standardized approach for the identification of patients with suspected infection may introduce variances in the proportion of infections that undergo proper investigation.
2. Lack of, or limited access to microbiological testing could exclude a significant proportion of the population with infectious syndromes that should be under surveillance. This limitation will result in the difficulty to obtain a representative sample of the population with AMR infections.
3. Late microbiological testing can lead to distorted rates. For instance, the testing may be done after initiation of antibiotic therapy. Likewise, in settings where microbiological sampling is not performed routinely, many patients may be tested only after antimicrobial treatment failures or when severely ill. This is likely to cause an ascertainment bias, with an overestimation of the true resistance burden within that population.
4. Inaccurate microbiological methods may distort the estimate of the frequency of infection or AMR which may lead to either over- or underestimation, depending on the direction of the inaccuracy.
5. Inaccurate interpretation of results, including lack of discrimination of true infections versus colonization or contamination. Some of the identified isolates may possibly represent cases of contamination of a specimen or colonization at a sampled site. Surveillance sites must take responsibility for assessing the clinical significance of positive cultures. However, some patients may have a combination of the bacteria causing infection and colonization and the laboratory may not be able to differentiate "true" pathogens from "colonizers". This is important to consider when interpreting the data as the number of reported isolates might be higher than those causing infections. Therefore, the prevalence of AMR infections might also be over- or underestimated, depending on whether susceptibility rates among the "colonizers" differ from those among the infecting pathogens and, if so, by how much.

GLASS has identified several complementary approaches to address these issues and to help achieve the representativeness of national or subnational data (Section 6).

5.4.2 Data limitations due to selective testing of pathogens and antimicrobial combinations under surveillance

The AST results for a specific antimicrobial could be missing due to selective testing defined by the facility guidelines. This includes second line/cascade testing (that is, when second-line antimicrobials are tested only on isolates resistant to first-line antibiotics) and "prescribing-specific" testing (that is, when only those antimicrobials that are specifically requested or currently used for treatment are tested). In addition, some laboratories may selectively report only a subset of the AST results to clinicians, for example, to encourage good antimicrobial stewardship. When selective reporting is applied in the context where most antimicrobials are routinely tested, surveillance reports should be generated from the full database of results for all antimicrobials that are routinely tested and not from the selectively reported data.

6 Approaches to improve data quality and representativeness

6.1 Enhancing the quality of surveillance based on routine diagnostic testing

Barriers to strengthening surveillance based on routine diagnostic testing include the absence of (or weak) diagnostic stewardship *(36)* procedures to identify patients with suspected infection and indications for laboratory tests; lack of access to laboratory tests to investigate the presence of infection, including culture and AST; weak laboratory capacity for testing; lack of (or weak) sample referral systems when laboratory testing is not available at the health care facility; and inaccurate and/or incomplete clinical data and reporting systems. Financial resources must be appropriately allocated to build these critical components of an effective patient care and surveillance system.

Each country should take a long-term view of surveillance and design a system that best fits current and projected needs. This system should be based on the capacity that is sustainable.

Steps to plan, evaluate and continuously review and expand a quality national surveillance system are addressed elsewhere *(30)*. As summarized below, GLASS suggests a progressive approach for establishing a well-functioning surveillance system.

1. Define the AMR surveillance objectives. For instance, if the country aims to assess the AMR frequency in hospitalized patients, then in-patient health care facilities should be targeted for the surveillance. If the national surveillance aims to assess AMR at all levels of health care, then the planning should include all levels of health care facilities in the country.
2. Health care facilities within the target population should be progressively included in the surveillance system to achieve a balanced distribution across all levels of health care and geographical locations.
3. Where there is capacity (for example, a sizeable number of facilities with access to diagnostics), probability sampling methods used for designing national surveys may help to guide the design of surveillance systems. Different approaches can be applied.
4. Develop and regularly train surveillance sites to promote the systematic identification and testing of patients with suspected infection, including microbial identification and AST. The training should also include ensuring that clinical and demographic data are complete. Undertake continuous monitoring to ensure that no patient with an indication for culture is missed and that patient data are complete. The AMR surveillance based on the systematic identification of infectious syndromes is also referred to as "syndrome-based" AMR surveillance *(3)* or "case-based" AMR surveillance *(41), (42).* It implies an active and systematic case-finding approach to identify all patients with signs and symptoms that meet the case definitions for the specific syndromes. This active prospective surveillance approach can more accurately reflect the incidence of resistant infections in the population under surveillance and may provide more precise data about the burden of AMR in the chosen setting. However, it is laborious and requires additional resources because of the need for detailed clinical information in addition to the laboratory results. At the same time, the benefit of using this approach goes beyond just quality surveillance data as it promotes quality of patient care.
5. Ensure consistency across surveillance sites and that the relevant departments and wards of each site are represented in the surveillance system as much as possible.
6. Identify, equip and train the surveillance sites' laboratories and enrol them into regular external quality assurance while closely monitoring their performance improvement.
7. In the absence of a clinical quality-assured laboratory in the surveillance site (health care facility), set up a proper sample referral system to ensure adequate patient care and quality of the microbiological data.
    a. Choose strategic geolocations for quality-assured laboratories to maximize diagnostic coverage of health care facilities across the country.
    b. Design and deploy rapid sample referral from surveillance sites to quality-assured laboratories, ensuring that transportation times are within recommended turn-around times.
8. Promote routine communication between clinicians, laboratory personnel, the infection prevention and control team and epidemiologists both at local and national levels.

6.2 Assessment of an AMR surveillance system based on routine diagnostic testing

The performance of national surveillance systems depends on several elements. These include a proper set-up of the surveillance core components, strengthening of the system for best patient care and appropriate AMR diagnostic stewardship[5], and access to quality health care to all citizens *(43)*. Each country should define the AMR surveillance development strategy and targets and monitor their progress.

Simple quantitative indicators can be used to tailor the applications of AMR surveillance data and to better target and inform country-specific interventions, such as epidemiological reviews, to help strengthen national AMR surveillance systems, based on the routine clinical sampling of patients seeking healthcare. These indicators can also help identify countries that may benefit from periodic surveys while they are planning and building the required systems. At the global level, GLASS proposes four high-level indicators (Table 6.1) to monitor a few performance features of national surveillance systems contributing AMR data to GLASS.

- Population-level indicator
- Healthcare level indicator
- Sampling indicator
- Laboratory performance indicator

As an initial step, these four indicators will focus on bloodstream infections. The rationale for starting this high-level monitoring focusing on infections relies on the following arguments: 1) bloodstream infections are associated with high morbidity and mortality *(44–46)*; and 2) WHO is the custodian of the new 3.d.2 indicator (AMR bloodstream infections *(47)*) under Target 3.d of the Sustainable Development Goals, which countries need to report to GLASS. These indicators will allow GLASS to conduct high-level monitoring of the performance of national surveillance systems over the years to detect AMR bloodstream infections. It should be noted that these high-level performance indicators are not designed to precisely identify the source of gaps in the quality, representativeness and accuracy of national data. Countries may apply additional methods for this purpose.

5 Appropriate diagnostic stewardship ensures that all patients with a suspected infection will have a sample taken and sent for identification where both bacterial isolation and AST will be carried out in quality-assured laboratories and performed following recognized international standards.

Table 6.1. High-level indicators of national surveillance systems contributing AMR data to GLASS

Population-level indicator	
Population - level indicators	**Method**
Expected bacterial bloodstream infection cases per 100,000 population (a)	Source for numerator (in order of priority): 1. Country assessment of bloodstream infection prevalence 2. Global burden of disease* 3. Systematic review of literature 4. Expert opinion Source for denominator (national population estimates): • https://population.un.org
Total bacterial bloodstream infection cases reported to GLASS per 100 000 population (b)	Source for numerator: • Data reported to GLASS • Source for denominator (national population estimates): • https://population.un.org
Indicator = observed versus expected	**(b/a) %**
Healthcare level indicator	
Healthcare level indicators	**Method**
Among the total count of hospitals in your country, the total count of patient-days of care in the surveillance calendar year (a)	Source: • National data
Among the total count of hospitals contributing data to GLASS, the total count of patient-days of care in the surveillance calendar year (b)	Source: • National data reported to GLASS
Indicator	**(b/a) %**
Sampling indicator	
Healthcare level indicators	**Method**
Expected number of patient-days with an indication for blood culture per 1,000 patient days (a)	Source: • Literature (expected cases); • Expert opinion
The observed number of patient days with blood culture reported to GLASS (b)	Source: • Total bacteriologically confirmed bloodstream infections reported to GLASS / 0.1
Indicator	**(b/a) %**
Laboratory indicator	
Healthcare level indicators	**Method**
Percentage of bacteriologically confirmed infections with AST result for at least one antibiotic (a)	Source: • GLASS data
Indicator	**(a) %**

* https://www.healthdata.org/gbd

** If it is estimated that only about 10% of sampled infections are bacteriologically confirmed.

6.3 National AMR prevalence surveys to improve the quality and representativeness of national AMR surveillance data (GLASS-AMR surveys)

Developing and sustaining a robust capacity for national surveillance through systematic continuous data collection and analysis from routine clinical activities remains challenging to ensure data quality and representativeness in many countries, particularly in those with the least resources. A main feature of the new GLASS phase is the implementation of national AMR surveys to complement surveillance based on routine diagnostic testing and inform its further development to improve the quality, completeness and representativeness of data.

The national AMR prevalence surveys involve periodic, strategic sampling of a population subset to overcome the paucity of high-quality representative AMR data originating from routine clinical practice in low-resource countries.

The method for GLASS-AMR surveys initially targets bloodstream infections. The full description of the GLASS method for national AMR prevalence surveys is provided elsewhere *(31)*. The main objectives and principles of this approach are described below.

6.3.1 Objectives of the national AMR prevalence surveys

The specific objectives of the national AMR prevalence surveys are as follows.

1. To estimate the national prevalence of AMR in hospitalized[6] patients with bacteriologically-confirmed community- or hospital-origin infections, following due consideration of relevant underlying factors (for example, documentation of antimicrobial therapy).
2. To implement a survey approach that accounts for the patient pathway within the health care setting when measuring prevalence and ultimately strengthens diagnostic stewardship and laboratory practice, thus minimizing the bias currently underlying AMR data from low- and middle-income countries,
3. To contribute to capacity-building and access to an appropriate diagnosis, treatment and care for people with drug-susceptible and drug-resistant infections.

6.3.2 Methodological principles of national AMR prevalence surveys

1. Cross-sectional survey following standardized methods that make it possible for the data to be comparable between settings and within settings over time, and following principles and standards for the ethical implementation of surveillance systems in public health.
2. Sample of hospitals selected using statistically meaningful probability sampling methods, irrespective of whether microbiology diagnostic services are available on site.
3. Application of a syndrome-based approach for the continuous active case finding of patients with suspected targeted infections in selected hospitals during an intake period, typically not exceeding 12 months (inclusion of all consecutive eligible patients).
4. Blood samples transported to the nearest quality-assured laboratory for microbiology and AST, carried out in line with international standards.
5. Minimum set of demographics and clinical information obtained for each patient in the survey.

The survey should be powered to estimate resistance with the desired precision for the most common organism in the target setting or GLASS target pathogens (for example, *Klebsiella pneumoniae*), taking the most conservative estimate for expected resistance for a particular antibiotic (that is, that approaching 50%), and the most conservative sample size that is operationally feasible. Data for less common pathogens identified from isolates will be collected opportunistically until the sample for the target bacterial species is reached. The sampling strategy to achieve sufficient power for the target analyses may include different approaches to fit the country context.

6 This could be extended to outpatients in the community in the future

7 GLASS-AMR surveillance targets

7.1 Specimen types and target pathogens

7.1.1 Priority specimen types

During the early implementation of GLASS, blood, urine, faeces (stool), and urethral and cervical swabs were included as priority specimen types for global AMR reporting. The underlying assumption is that the isolation of a target pathogen from routine samples of one of these specimens would indicate the presence of infection in the bloodstream, urinary tract, gastrointestinal tract or urogenital tract (gonorrhoea), respectively. Infections in these anatomical sites are common and an alarming increase has been observed in resistance to drugs of "last resort" used to treat infections in these sites in some countries.

Isolation of bacteria from blood specimens is usually indicative of a true infection as long as no contamination occurs during the collection process, especially when focusing on specific pathogens, such as GLASS target pathogens for example. Some organisms can always be considered pathogens when isolated from certain sites, such as *Salmonella* spp. from faeces or *N. gonorrhoeae* from urethral or cervical swabs. Given that some associations between pathogen isolation and clinical infection are less clear cut (for example, in urine samples), GLASS-AMR relies on a clinical indication for sampling to reduce the number of false positives. While patients with uncomplicated urinary tract infection may not be routinely sampled, resulting in overestimated resistance rates, they can still provide an indication of emerging resistance in gram-negative bacteria in the community.

To better address important public health threats, the next period of GLASS implementation has added additional specimen categories. These include CSF for the surveillance of AMR in bacterial meningitis pathogens, specimens from the lower respiratory tract for the surveillance of AMR in pathogens causing pneumonia, and non-urogenital samples (rectal and pharyngeal) for the surveillance of AMR in *N. gonorrhoeae*. The full list of selected specimen types and pathogens is shown in Table 7.1.

Other important sites of infection may be included in later stages. At the same time, it should be noted that **countries should include the sites of infection, pathogens and antimicrobials that are considered to be national priorities for surveillance**, in addition to the specimens and pathogens targeted by GLASS. It should also be noted that countries developing their AMR surveillance systems are not expected to report all specimen types from the beginning. A stepwise approach could be considered, starting from blood samples and adding urine and other specimens at a later stage, especially those that pose methodological difficulties.

7.1.1.1 Blood

Isolation of a pathogen from blood (as opposed to a contaminant) indicates the presence of a bloodstream infection and is a diagnostic test recommended for every patient with sepsis, a life-threatening condition, even if treatment with appropriate antibiotics is initiated rapidly. Organisms typically considered as commensals may also cause bloodstream infections, but their significance can only be determined when two sets of blood cultures have been drawn from different sites within a specified timeframe and they are isolated from both sets. Ideally, routine blood culture should include two sets of cultures (each set consisting of an aerobic and anaerobic bottle if the laboratory is capable of isolating and identifying anaerobes) from two different venipuncture sites drawn 5 minutes apart after careful disinfection of the skin. If this is not possible, one set may be drawn from aspiration via an existing intravascular device, although this increases the risk for contamination. Isolation of a primary pathogen in a single set or of the same commensal in two culture sets suggests a significant finding.

7.1.1.2 CSF

CSF has been added as a priority specimen type in the second phase of GLASS in order to detect emerging resistance in primary pathogens causing community-acquired bacterial meningitis *(N. meningitidis, Haemophilus influenzae, Streptococcus pneumoniae)* and gram-negative bacteria responsible mostly for healthcare-associated infections and meningitis in neonates. CSF cultures should ideally be combined with simultaneous blood cultures as meningitis caused by bacterial pathogens is usually associated with the onset of bacteremia. When the CSF punctate is collected (under aseptic conditions) into numbered tubes, the first tube should not be used for culture due to a higher probability of skin contaminants and tube no. 3 is frequently reserved for culture.

7.1.1.3 Urine

A midstream, clean catch urine sample is the specimen of choice to detect urinary tract infection, although poorly taken urine samples, particularly from women and children, can be prone to contamination with faecal, skin and normal vaginal microbiota. The laboratory should have standard algorithms in place to assess the likelihood of the clinical significance of isolated organisms using purity of culture and colony counts. For example, samples with a growth of more than two pathogens in significant numbers, even if one is *E. coli* or *K. pneumoniae*, should be excluded as there is a high probability of contamination and the clinical significance is uncertain.

Microbiology laboratories should have interpretation and reporting protocols for urinary tract infections in specific patient groups, including children, pregnant women, the elderly, and those with an indwelling urinary catheter. In GLASS-AMR, only significant colony counts of the primary pathogens, that is *E. coli* (10^5 colony-forming units [cfu]/mL) and *K. pneumoniae* (10^5 cfu/mL) should be included, although other pathogens may be relevant for patient management and local and national surveillance.

7.1.1.4 Stool

Diarrhoeal disease is a major cause of morbidity and mortality globally. Shigella spp. and non- typhoidal *Salmonella* are important bacterial causes of diarrhoeal disease, but these organisms are not part of the normal stool microbiota. Growth of these pathogens in stool samples is therefore a diagnostic indicator of diarrhoeal disease. It should be noted that typhoidal salmonellae, although present and excreted in faeces, are most importantly detected in blood cultures as they cause systemic disease (fever and malaise) and may not be associated with diarrhoeal illness.

7.1.1.5 Specimens from the lower respiratory tract

Although bacterial respiratory tract infections are common, respiratory tract samples were not included in the early implementation of GLASS because of the difficulty in ascertaining the significance of pathogens when mixed with upper respiratory tract normal microbiota or other colonizers. This requires skill, experience, and a good liaison communication with the requesting clinicians.

Secondary bacterial pneumonia is well recognized as a complication in post-viral influenza-like illness. During the coronavirus disease (COVID-19) pandemic, a considerable number of hospitalized patients treated for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) respiratory illness suffered morbidity and mortality associated with secondary bacterial infection *(48,49)*. Therefore, respiratory samples have been included in the next phase of GLASS, despite difficulties in obtaining representative samples from the lower respiratory tract.

Recovery and recognition of organisms responsible for pneumonia depends on the following:

- adequacy of the lower respiratory tract specimen;
- avoidance of contamination by upper respiratory tract commensals;
- use of both microscopy techniques and culture methods;
- knowledge of current and recent antimicrobial treatment.

The distinction between tracheobronchial colonization and true pulmonary infection can prove to be difficult.

Representative specimens from the lower respiratory tract include bronchial aspirate, transthoracic aspirate, bronchoalveolar lavage, transtracheal aspirate, bronchial brushings, protected catheter specimens, bronchial washings, endotracheal tube specimens in intubated patients (with the same contamination limitations as sputum specimens) *(50)*, and expectorated sputum. Expectorated sputum samples are known to have significant issues with contamination. Early-morning sputum samples are preferred because they contain pooled overnight secretions in which pathogenic bacteria are more likely to be concentrated.

Gram stains on sputum specimens may be used for determining the quality of the specimen and for predicting likely pathogens by their characteristic appearance. Determining the quality of the specimen is based on the number of polymorphonuclear leucocytes and squamous epithelial cells present: purulent specimens may be selected for culture and non-purulent specimens or specimens contaminated with squamous epithelial cells may be rejected. The sensitivity of Gram stain can vary and is generally low and often dependent on the individual reviewing the slide. Culture methods should follow standard protocols as defined by the local laboratory and only be performed on representative samples.

If non-representative samples are cultured there is a risk that contaminants will be processed and reported, thus causing a major bias in the surveillance data collected. Furthermore, reporting of non-significant (and potentially multi-resistant) gram-negative colonizers will drive the inappropriate use of broad-spectrum antibiotics and further promote the selection of multi-drug resistant bacteria.

GLASS will discourage countries from reporting data from respiratory samples if contamination could not be reliably differentiated from true pathogens.

7.1.1.6 Specimen types for the surveillance of AMR in gonococci

N. gonorrhoeae is one of the pathogens in which antibacterial resistance has developed so extensively that there are very limited treatment options left in some countries. Gonococcal infections can occur in different anatomical sites according to sexual practices. To align *N. gonorrhoeae* surveillance in GLASS with several already existing vertical programmes, microbiological reports concerning samples from two body sites other

than urogenital specimens (urethral and cervical swabs) are now included in GLASS-AMR, that is, rectal and pharyngeal swabs.

7.1.2 Target pathogens

The pathogens initially selected for reporting to GLASS were chosen to cover common bacterial infections associated with health care as well as community-acquired infections. The selection covers pathogens causing a number of life-threatening infections, foodborne infections and infections where there are virtually no treatment options left. Pathogens were selected based on their public health burden, particularly if they develop multi-drug resistance. Multidrug-resistant organisms can result in significant harm to individuals and are a burden to healthcare systems and economies. Other pathogens (for example, *Salmonella* spp., *Shigella* spp.) were selected because they cause infections that lead to significant morbidity and mortality in low- and middle-income countries.

In this manual, additional pathogens have been included for surveillance. These include bacteria affecting vulnerable populations (for example, *H. influenzae*, which can cause severe infections in children) and several of the GLASS target pathogens that are included in the WHO *Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics* published in 2017 *(51)*. According to the ranking applied in the prioritization process, four GLASS target pathogens are considered to be a critical priority, including *Acinetobacter* spp. and *P. aeruginosa* resistant to carbapenems and *E. coli* and *K. pneumoniae* resistant to carbapenems or third-generation cephalosporins. A further three pathogens also belong to the high priority group (methicillin-resistant *Staphylococcus aureus*, fluoroquinolone-resistant *Salmonella* spp., and *N. gonorrhoeae* resistant to third-generation cephalosporins or azithromycin). Penicillin non-susceptible S. *pneumoniae* and fluoroquinolone-resistant *Shigella* spp. are medium priorities according to the 2017 list.

GLASS focuses on some of the most important pathogens for surveillance at the global level, and during the next implementation stage, the GLASS IT platform (a web-based platform for global data sharing on AMR) will only gather data on the specimen types and pathogens included in this manual. However, priorities for local and national surveillance may include other organisms and antimicrobial agents and should be addressed properly, even though they are not yet requested to be reported in GLASS.

The updated list of target pathogens and specimens selected by GLASS for the global reporting of AMR surveillance is shown in Table 7.1.

Table 7.1. GLASS target pathogens and specimen types

Target pathogens*	**Specimens**					
	Blood	CSF	Urine	Stool	**Lower respiratory tract**	Urethral, cervical, **rectal, and pharyngeal** swabs
Acinetobacter spp.	●	○			●	
E. coli	●	○	●		○	
K. pneumoniae	●	○	●		●	
P. aeruginosa	●	○			●	
S. aureus	●	○			●	
S. pneumoniae	●	●			●	
N. meningitidis	●	●				
H. influenzae	○	●			●	
Salmonella spp. (non-typhoidal)	●	○		●		
***Salmonella* enterica serovar Typhi**	●			○		
***Salmonella* enterica serovar Paratyphi A**	●			○		
Shigella spp.				●		
N. gonorrhoeae						●

● Data collected and included in the official GLASS report when available.
○ Included in the GLASS database to accommodate data when submitted, but not necessarily included in the annual GLASS report.
* New target pathogens and specimens are marked in bold font

7.2 Antimicrobial-pathogen combinations

Antimicrobials have been selected to allow for the detection of the possible presence of the most important antibiotic resistance mechanisms for each target pathogen. While a relatively limited number of antimicrobial agents is included, information gleaned from the surveillance data can be extrapolated (based on known resistance mechanisms) to other classes of antimicrobials. Consideration is given also to antimicrobials that are commonly used and available locally and nationally in participating countries. Among 32 antimicrobial drugs selected for global surveillance purposes, 11 are classified as "Access", 18 belong to the "Watch" group, and 3 are "Reserve" antibiotics, according to the WHO AWaRe classification of antibiotics *(52)*. Eighteen of the selected antibiotics are included in the current WHO Model Lists of Essential Medicines *(33)*. The full list of the antimicrobial-pathogen combinations covered by GLASS is provided in Table 7.2.

When using Table 7.2, it is important to clearly understand the following:

- Table 7.2 provides the list of target antimicrobial-pathogen combinations selected by GLASS-AMR for global surveillance purposes. **The list is not intended to guide testing or prescribing practices.**
- The list does not imply that all of the included antimicrobials should be routinely included in AST by clinical laboratories. However, if susceptibility testing to any of these antimicrobials is performed, the results should be reported to GLASS. Similarly, the list does **not** mean that these are the only antimicrobials recommended for routine AST for the organism/body site combination. Please refer to your local guidelines and international standards for recommendations.
- While an attempt was made to select a small number of representative drugs for each antimicrobial group, there are similar drugs in the same categories (for example, multiple third-generation cephalosporins or carbapenems). This was done on purpose as different laboratories in different countries will often test just one of the drugs in a group, and a laboratory may change which drug is tested over time. This approach allows users and GLASS to meaningfully combine data from different laboratories that test different drugs within each antimicrobial group.

7.2.1 Subgroups of antimicrobials

AMR may need to be analysed both for a single antimicrobial and for a group of similar antimicrobial drugs. Grouping can be done with antimicrobials from the same class so as to better detect important resistance phenotypes, or with antimicrobials from different classes to recognize and track multidrug-resistant phenotypes *(41)*. Collection of individual-level data (Section 8.2) allows for both grouping options.

GLASS priority subgroups are presented in Annex 3 using the Anatomical Therapeutic Chemical (ATC) classification system *(53)* to define and code the subgroups. Use of this classification will also facilitate the integrated analysis of AMR data and data on national antimicrobial drug consumption, as consumption data are often reported using ATC subgroups only.

7.3 Molecular targets

During the next implementation period, GLASS will continue to collect phenotypic test results, but also gradually introducing molecular methods *(54)*, including whole genome sequencing (WGS) *(55)* results, and planning their implementation on a systematic basis for the mid- and long-term GLASS development stages. For the next implementation period, an option for submission of data generated by molecular AMR diagnostics will be offered to countries to complement phenotypic AMR diagnostics data and improve understanding of the underlying mechanisms responsible for resistance. They will still need to be made part of the primary data sets. The molecular targets are listed in Annex 7.

Table 7.2. Specimens, pathogens, and antimicrobial drugs selected for the global surveillance of AMR

Specimen	Laboratory case definition	Pathogens under surveillance	Antimicrobial group (ATC)	Antimicrobials to report to GLASS if tested [a]
Blood	Isolation of pathogen from blood [b]	*Acinetobacter* spp.	Tetracyclines	Tigecycline, minocycline
			Aminoglycosides	Gentamicin, amikacin
			Carbapenems [c]	Imipenem, meropenem, doripenem
			Polymyxins	Colistin
		E. coli and *K. pneumoniae*	Sulfonamides and trimethoprim	Co-trimoxazole
			Fluoroquinolones	Ciprofloxacin, levofloxacin
			Third-generation cephalosporins	Ceftriaxone, cefotaxime, ceftazidime
			Fourth-generation cephalosporins	Cefepime
			Carbapenems [c]	Imipenem, meropenem, ertapenem, doripenem
			Polymyxins	Colistin
		P. aeruginosa	Third-generation cephalosporins	Ceftazidime
			Combinations of penicillins, including beta-lactamase inhibitors	Piperacillin/tazobactam
			Aminoglycosides	Gentamicin, amikacin, tobramycin
			Carbapenems [c]	Imipenem, meropenem, doripenem
			Polymyxins	Colistin
		S. aureus	Beta-lactamase resistant penicillins	Oxacillin
			Second-generation cephalosporins	Cefoxitin [d]
		S. pneumoniae	Beta-lactamase sensitive penicillins	Penicillin G
			Beta-lactamase resistant penicillins	Oxacillin [e]
			Third-generation cephalosporins	Ceftriaxone, cefotaxime
			Sulfonamides and trimethoprim	Co-trimoxazole
			Macrolides	Erythromycin

Specimen	Laboratory case definition	Pathogens under surveillance	Antimicrobial group (ATC)	Antimicrobials to report to GLASS if tested [a]
		Salmonella spp.[f]	Fluoroquinolones	Ciprofloxacin, levofloxacin
			Third-generation cephalosporins	Ceftriaxone, cefotaxime, ceftazidime
			Carbapenems [c]	Imipenem, meropenem, ertapenem, doripenem
		Salmonella enterica serovar Typhi and *Salmonella enterica* serovar Paratyphi A	Amphenicols	Chloramphenicol
			Penicillins with extended spectrum	Ampicillin
			Sulfonamides and trimethoprim	Co-trimoxazole
			Fluoroquinolones	Ciprofloxacin, levofloxacin
			Third-generation cephalosporins	Ceftriaxone, cefotaxime, ceftazidime
			Macrolides	Azithromycin
CSF	Isolation of pathogen from cerebrospinal fluid	*S. pneumoniae*	Beta-lactamase sensitive penicillins	Penicillin G
			Beta-lactamase resistant penicillins	Oxacillin e
			Third-generation cephalosporins	Ceftriaxone, cefotaxime
			Sulfonamides and trimethoprim	Co-trimoxazole
		N. meningitidis	Beta-lactamase sensitive penicillins	Penicillin G
			Rifamycins	Rifampicin
			Fluoroquinolones	Ciprofloxacin
			Third-generation cephalosporins	Ceftriaxone, cefotaxime
		H. influenzae	Penicillins with extended spectrum	Ampicillin
			Combinations of penicillins, including beta-lactamase inhibitors	Amoxicillin-clavulanic acid
			Third-generation cephalosporins	Ceftriaxone, cefotaxime
			Sulfonamides and trimethoprim	Co-trimoxazole
Urine	Significant growth in urine specimen [g]	*E. coli* and *K. pneumoniae*	Nitrofuran derivatives	Nitrofurantoin (for *E. coli*)
			Penicillins with extended spectrum	Mecillinam
			Sulfonamides and trimethoprim	Co-trimoxazole
			Fluoroquinolones	Ciprofloxacin, levofloxacin
			Third-generation cephalosporins	Ceftriaxone, cefotaxime, ceftazidime
			Fourth-generation cephalosporins	Cefepime
			Carbapenems [c]	Imipenem, meropenem, ertapenem, doripenem
			Polymyxins	Colistin

Specimen	Laboratory case definition	Pathogens under surveillance	Antimicrobial group (ATC)	Antimicrobials to report to GLASS if tested [a]
Stool	Isolation of *Salmonella* spp.[h] or *Shigella* spp. from stool	*Salmonella* spp.	Sulfonamides and trimethoprim	Co-trimoxazole
			Fluoroquinolones	Ciprofloxacin, levofloxacin
			Third-generation cephalosporins	Ceftriaxone, cefotaxime, ceftazidime
			Carbapenems [c]	Imipenem, meropenem, ertapenem, doripenem
		Shigella spp.	Sulfonamides and trimethoprim	Co-trimoxazole
			Fluoroquinolones	Ciprofloxacin, levofloxacin
			Third-generation cephalosporins	Ceftriaxone, cefotaxime, ceftazidime
			Macrolides	Azithromycin
Lower respiratory tract	Significant growth in representative sputum samples or in material obtained from lower respiratory tract by the procedures listed in Section 7.1.1.5	*S. pneumoniae*	Beta-lactamase sensitive penicillins	Penicillin G
			Beta-lactamase resistant penicillins	Oxacilline
			Third-generation cephalosporins	Ceftriaxone, cefotaxime
			Sulfonamides and trimethoprim	Co-trimoxazole
		H. influenzae	Penicillins with extended spectrum	Ampicillin
			Combinations of penicillins, including beta-lactamase inhibitors	Amoxicillin-clavulanic acid
			Third-generation cephalosporins	Ceftriaxone, cefotaxime
			Fluoroquinolones	Ciprofloxacin, levofloxacin
			Sulfonamides and trimethoprim	Co-trimoxazole
		S. aureus	Beta-lactamase resistant penicillins	Oxacillin
			Second-generation cephalosporins	Cefoxitin [d]
		Acinetobacter spp.	Tetracyclines	Tigecycline, minocycline
			Aminoglycosides	Gentamicin, amikacin
			Carbapenems [c]	Imipenem, meropenem, doripenem
			Polymyxins	Colistin

Specimen	Laboratory case definition	Pathogens under surveillance	Antimicrobial group (ATC)	Antimicrobials to report to GLASS if tested [a]
		E. coli and *K. pneumoniae*	Sulfonamides and trimethoprim	Co-trimoxazole
			Fluoroquinolones	Ciprofloxacin, levofloxacin
			Third-generation cephalosporins	Ceftriaxone, cefotaxime, ceftazidime
			Fourth-generation cephalosporins	Cefepime
			Carbapenems [c]	Imipenem, meropenem, ertapenem, doripenem
			Polymyxins	Colistin
		P. aeruginosa	Third-generation cephalosporins	Ceftazidime
			Combinations of penicillins, including beta-lactamase inhibitors	Piperacillin/tazobactam
			Aminoglycosides	Gentamicin, amikacin, tobramycin
			Carbapenems [c]	Imipenem, meropenem, doripenem
			Polymyxins	Colistin
Urethral, cervical, rectal, pharyngeal swabs	Isolation of *Neisseria gonorrhoeae*	*N. gonorrhoeae*	Third-generation cephalosporins	Ceftriaxone, cefixime
			Macrolides	Azithromycin
			Aminocyclitol	Spectinomycin
			Fluoroquinolones	Ciprofloxacin
			Aminoglycosides	Gentamicin

[a] The listed substances are priorities for the surveillance of resistance in each pathogen, although they may not be first-line options for treatment. One or more of the drugs listed may be tested. AST results and numerator and denominator data for each drug will be reported separately

[b] Any pathogen isolated from a blood culture may be significant for local and national surveillance; only the pathogens selected for global surveillance are listed here

[c] Imipenem or meropenem is preferred to represent the group when available.

[d] Recommended for the detection of methicillin resistance in *S. aureus* when using disk diffusion testing.

[e] Oxacillin disk testing is a screening for reduced susceptibility or resistance to penicillin.

[f] Not serovar Typhi or Paratyphi A.

[g] Urinary catheter samples should be excluded if possible.

[h] Discriminate between serovar Typhi or Paratyphi A whenever possible. Data collected and included in the official GLASS report when available.

8 Annual AMR data submission to GLASS

On an annual basis, countries enrolled in GLASS report data generated through their routine surveillance systems to WHO, including both AMR rates and information on the status of implementation of their surveillance systems. Regarding AMR rates, GLASS-AMR accepts the submission of aggregated and individual-level data.

8.1 Aggregated data

Two datasets are requested to be submitted to GLASS (see Table 8.1).

1. **RIS dataset** with susceptibility testing results. These are data (aggregated from all participating national surveillance sites' submissions) on the number of **R**[7], **I**[8], **S**[9] isolates for each target antimicrobial detected in GLASS priority specimens, stratified by gender, age group and infection origin.
2. **SAMPLE dataset** with the number of tested patients. These are the numbers of patients from whom specimens have been taken and sent to the laboratory for bacterial isolation purposes, stratified by gender, age group and infection origin (as in the *RIS* dataset).

Both the *RIS* and *SAMPLE* datasets should be generated from the same source database. Countries can submit a SAMPLE dataset with a *RIS* dataset, or a *RIS* dataset alone.

For GLASS reporting purposes, all variables in the datasets are mandatory and they should always be present. When patient demographic and epidemiological data are not available (gender, age or infection origin), a "UNK" value must be entered. Users can manually input "UNK" values, or use applications for data management and analysis, such as WHONET, which automatically generates the "UNK" values for missing data.

Concerning previously mentioned isolate- and sample-based data approaches (Section 5.2.1), Table 5 describes how the two datasets provide the needed information. All patients included in the RIS dataset must be also represented in the SAMPLE dataset, as the latter includes the information on the whole target population. Conversely, as the SAMPLE dataset includes also information on patients with no bacterial growth, the *RIS* dataset will always include a lower number of patient data.

7 **R** = Resistant

8 **I** = Susceptible, Increased exposure (EUCAST) or Intermediate (CLSI)

9 **S** = Susceptible

Table 8.1. Datasets reported using the two surveillance approaches

Data collected	AMR surveillance approach	
	Isolate-based	**Sample-based**
Patients' AST results for bacterial pathogens and antibiotics under surveillance	RIS **dataset**	RIS **dataset**
Numbers of patients from whom samples have been collected for microbiological testing (both with and without growth of the bacterial pathogens under surveillance) according to specimen type		*SAMPLE* **dataset**

8.1.1 RIS dataset

Data included in the *RIS* dataset are listed below:

- reporting country
- year of data collection
- specimen type
- pathogen
- gender
- infection origin (community vs. hospital as proxy for infection onset)
- age group
- antimicrobial used for AST
- number of R isolates
- number of I isolates
- number of S isolates
- number of isolates with AST results not reported (not performed) for a specific antibiotic
- number of isolates with AST performed but no interpretation of results available
- subset of national aggregated data

A detailed description of the variables in the *RIS* dataset is available in the Annex 1.

8.1.2 SAMPLE dataset

The *SAMPLE* dataset is collected to generate sample-based data and contains denominator data organized using the same aggregation and stratification approaches as for the *RIS* file. To create a stratified *SAMPLE* file, the source database needs to contain the number of patients with all positive (that is, both with growth of GLASS and non-GLASS pathogens) and negative (no growth) results and with all GLASS variables present (gender, age and infection origin). The *SAMPLE* dataset **cannot** be generated if only the number of patients with positive species identification results is available, without the number of negative tests.

Note that the dataset contains only the number of patients for which samples were sent to the laboratory for bacterial isolation purposes and not for other reasons. For example, stool specimens are often taken for "ova and parasites". Similarly, many genital samples are collected for the diagnosis of vaginosis/vaginitis by microscopy, not for the culture of *N. gonorrhoeae*, which requires special media and growth conditions. Therefore, if these patients were to be included in the dataset, they would incorrectly increase the denominator of cultured patients, which is a proxy for patients showing symptoms of a bacterial infection.

Data included in the *SAMPLE* dataset are listed below:

- reporting country
- year of data collection
- specimen type
- gender
- infection origin (community vs. hospital as proxy for infection onset)
- age group
- number of patients from which a sample is taken
- number of patients with positive sample for GLASS pathogens
- number of patients with positive sample for non-GLASS pathogens
- number of patients with negative sample
- subset of national aggregated data

A detailed description of the variables in the *SAMPLE* dataset is available in Annex 2.

8.2 Individual-level data

GLASS-AMR offers the option of submitting individual, line-listed, anonymized AMR data to participating countries. It should be noted that the same variables collected in the individual-level data are also collected for the national AMR prevalence surveys (GLASS-AMR surveys). This alignment facilitates GLASS-AMR surveys in countries with ongoing routine surveillance to complement and inform improvement of the latter.

Apart from allowing for better data validation and management, the huge benefit associated with individual data is their analytical potential. Specifically, individual-level data can allow to:

- monitor the occurrence of multidrug resistance, critical for informing research and development of new therapeutic and diagnostic tools;
- explore additional data analyses and stratifications;
- generate state/province or regional statistics by including facility identifiers to support an analysis of data by national surveillance systems;
- analyse drivers and risk factors linked to resistance;
- enhance the ability to study the evolution of resistance during the year;
- improve capacity for outbreak detection;
- generate transmission trends, using both spatial and genetic information;
- provide several additional ways to assess data quality.

At the same time, GLASS-AMR will continue collecting national aggregated data, which will still offer a valuable set of information regarding the proportion and frequency of AMR within a given population. In addition, once its limitations are understood, data can be used to obtain meaningful insight into the development of resistance in enrolled countries. However, the aggregation of AMR data at national levels poses a major challenge for accurate data analysis and interpretation of results.

A number of countries are already submitting individual-level data to several international networks supporting GLASS such as the Central Asian and European Surveillance of Antimicrobial Resistance Network (CAESAR) *(56)*, the European Antimicrobial Resistance Surveillance Network (EARS-Net) *(57)*, and the *Red Latinoamericana de Vigilancia de la Resistencia a los Antimicrobianos* (ReLAVRA; Latin American Network for Antimicrobial Resistance Surveillance) *(58)*. The individual data module has been developed in the GLASS IT platform and is available to all countries that wish to explore the benefits of individual data submission, including the validation and analytical tools built into the platform.

8.2.1 Individual-level dataset

The individual-level dataset includes both the AST interpretations (R, I, S) and "raw" AST measurements (disk zone diameters or minimum inhibitory concentration [MIC] values) and has all the variables required to generate the GLASS aggregated dataset, as well as additional technical and epidemiological variables.

All patient-specific identifiers in the individual-level dataset are anonymized to avoid identification of individual patients. Data included in the individual-level dataset are as follows:

- year
- reporting country
- reporting region
- laboratory identifier (will be encrypted by the NCC before reporting to GLASS)
- healthcare facility identifier (will be encrypted by the NCC before reporting to GLASS)
- hospital department (see Annex 4)
- anonymized patient identifier
- gender
- age
- patient location type (inpatient[10] vs. outpatient [11])
- date of admission
- date of specimen collection
- specimen type
- isolate identifier
- pathogen
- antimicrobial used for AST
- AST results (zone diameters and interpretations, minimum inhibitory concentrations (MICs) and interpretations, gradient strip testing results and interpretations)
- final interpretation of AST results (R, I, S, etc.)
- guidelines used for susceptibility testing (CLSI, EUCAST, etc.)

8.2.2 Collection of additional denominators for the individual-level dataset

In addition to the variables listed in Section 8.2.1, countries reporting individual data are requested to also submit data on population denominators and characteristics of the participating surveillance sites, including the following information:

At the national level:

- total national population in the reporting year (based on the United Nations Population Division estimates).

10 A person who is formally admitted to a health care facility and who is discharged after one or more days

11 A person who goes to a healthcare facility for diagnosis or treatment, but who does not require to be admitted for an overnight stay

Per surveillance site:

- numbers of patients seeking care during the reporting year at surveillance sites;
- number of consultations in outpatient clinics for the reporting year;
- total number of patient admissions for inpatient facilities for the reporting year;
- type of the facility (hospital versus outpatient clinic);
- level of care for the hospitals (primary, secondary, tertiary) (see Annex 5 for types of care);
- best estimate of the catchment population of the healthcare facility in the reporting year;
- hospital size in number of beds in the reporting year;
- number of intensive care beds in the reporting year;
- total number of patient days in the hospital in the reporting year;
- total number of blood culture requests (sets)[12] per year;
- total number of patients with suspected bloodstream infection for which blood culture was requested per year;
- total number of blood specimens received by the laboratories per year.

8.3 Collection of data on the status of national surveillance system

GLASS will continue to collect data on the status of national AMR surveillance systems using the GLASS implementation questionnaire (Annex 6), together with the collection of indicators to define the representativeness and quality of the AMR surveillance data.

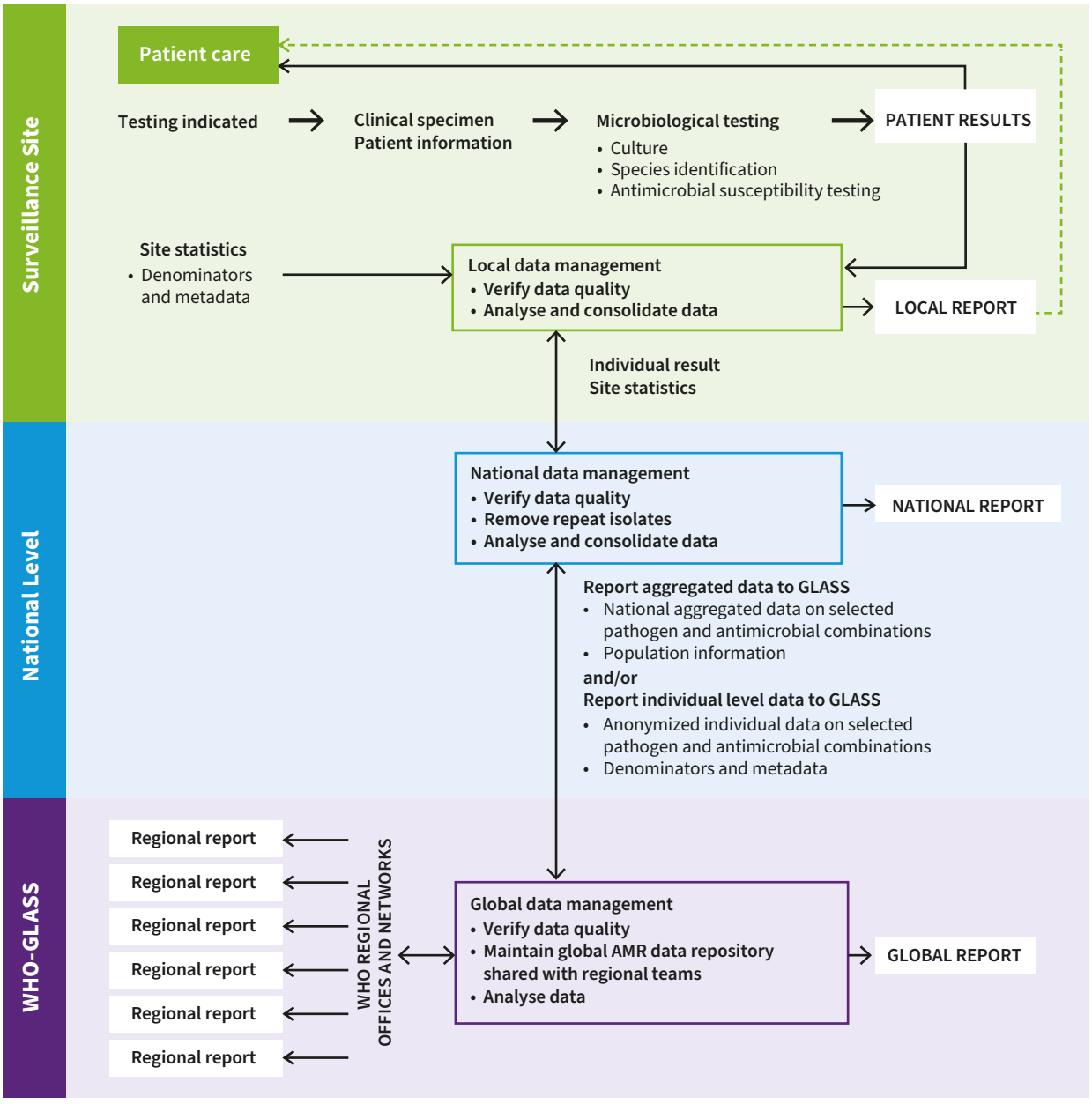
12 One request/set consists of any number of blood culture bottles that are taken from one patient on a single occasion for diagnostic purposes

9 Collection, management, analysis and reporting of data

9.1 GLASS data flow

A schematic view of the AMR data flow is shown in Fig. 9.1 and described below.

Fig. 9.1. GLASS data flow



9.2 Collection and management of data at surveillance sites

Clinicians at the participating health care facilities should be trained and encouraged to send samples for culture and AST from patients with suspected infection to the laboratory serving the health care facility/surveillance site. While sampling of all patients with suspected infection may not happen in many places, an effort should be made to introduce health care facilities to the concept of diagnostic stewardship, which comprises coordinated guidance and interventions to improve the use of microbiological diagnostics to guide therapeutic decisions *(36)*. Appropriate and timely diagnostic testing, including specimen collection, pathogen identification and AST, as well as the accurate and timely reporting of clinically relevant results must be promoted in all health care facilities. The underutilization and incorrect use of microbiological tests and diagnostic tools has a negative effect on the management and outcome for individual patients. It may also lead to a selection bias and result in a lack of representative and reliable surveillance data for empiric treatment recommendations and AMR control strategies.

Surveillance sites should have responsible personnel who are trained in collecting, analysing and reporting epidemiological, clinical and laboratory data. This includes the capacity to understand and analyse basic demographic information from the population covered by the surveillance site, to organize and analyse data manually or by means of an informatics tool, and to produce timely reports and feedback on a regular basis.

The very minimum core patient data required by GLASS that should accompany any request for AST are as follows: unique identifier; age; gender; specimen type; date of specimen collection; date of admission; and patient location type status (inpatient vs. outpatient). The last two are important to define the origin of the infection. Additional information may be requested according to local and national protocols and when reporting individual-level data to GLASS (for example, hospital name, ward or department, patient diagnosis, medical history, referral, antimicrobial therapy, etc.).

To implement the sample-based approach, data associated with the sample should be registered (added where hospital information systems are in use) using data management software as soon as the request is generated and before the species identification and AST results are available, irrespective of these results being negative or positive. These results should be added to the database serving as a repository for surveillance data for all specimen types and all pathogens and antimicrobials relevant for the surveillance site, without limiting the list by the GLASS targets or the targets defined by a national programme.

For sites that do not yet have suitable software for efficient data management and reporting in place, the freely-available WHONET software *(59)* is recommended. WHONET can be used on stand-alone computers or be linked to existing information systems and includes a feature for exporting AMR statistics into the format required for producing local and national reports and for uploading to the GLASS IT platform.

9.3 Laboratory procedures at surveillance sites

On-site laboratory capability and capacity for testing specimens facilitates surveillance, but is not essential if the site can store and transport samples rapidly to another testing facility serving the site. All surveillance sites must be linked to at least one laboratory that can identify the pathogens and perform AST in time according to international standards. Specimen collection, culture and species identification must be performed according to good laboratory practice as described in WHO manuals *(60,61)* and textbooks and as recommended by the NRL. For AST, the disk diffusion methods recommended by the CLSI *(62)* or EUCAST *(63)*, or automated, semi-automated or manual testing for MICs and gradient diffusion can be used. The latest published clinical breakpoints should be applied. All methods should be internationally recognized and selected based on the available resources and sustainability considerations. With the aggregated data collection, GLASS will collect only susceptibility data interpretations categorized as “R”, “I” and “S”. However, it recommends that MICs or inhibition zone diameters are also collected and reported at national level whenever possible to allow quality control of data, comparison of old and new results, and to track microbiological subpopulations in outbreak investigations, etc. The information on which interpretive criteria are being applied is collected by GLASS-AMR for the reporting country (aggregated data) and for the participating surveillance sites (individual-level data).

Staff should be trained to recognize any unusual or unexpected findings from routine microbiology species identification and AST results and raise alerts if necessary. When a new drug is introduced into clinical practice, laboratories should routinely test susceptibility to the drug in order to identify emerging resistance.

Some of the isolates identified, particularly mixed flora, may represent cases of contamination of specimens or colonization at the sampled body site. Surveillance sites are responsible for assessing the clinical significance of positive cultures and to identify and exclude contaminants from their data. Therefore, positive cultures reported are considered a proxy for infection.

Laboratories serving participating surveillance sites should use a quality management system recognized by the NRL to assure the accuracy, reliability and timeliness of reported results. All aspects of laboratory testing required to isolate and identify an infectious agent and to detect resistance must be controlled for quality according to the appropriate WHO manuals *(64,65)* and CLSI *(66)* or EUCAST *(67)* guidelines. All laboratories that provide data to an AMR surveillance system must

participate in at least one proficiency testing scheme that is recognized by the NRL and covering AST. Corrective actions should be promoted by the NRL and based on findings from external quality assessment programmes.

9.4 Collection and management of data at the national level

The NCC receives standardized datasets from the local surveillance sites and reports the data to GLASS. In addition to the datasets required by GLASS, a more comprehensive approach is recommended at the national and local levels, including other species and specimen types according to national policy.

For data originating from routine surveillance, the most common surveillance period and also recommended by GLASS is one year. Collecting the data over one year provides a more representative sample and decreases the impact of outbreaks or seasonal variations on the observed AMR rates. Data generated through national AMR prevalence surveys can also be reported to GLASS, based on the periodicity of the surveys.

In particular, management of data at the national level includes quality checks, removal of duplicated results, encryption, generation of aggregated data files and submission of the data to GLASS.

9.5 Checking quality of data at the local level

It is expected that the local surveillance sites will perform periodic quality checks on collected data before submitting them to the national level. The data will need to be assessed for completeness including 100% completeness of mandatory variables, and checked for consistency and plausibility, as well as adherence to national standards for microbiological species identification and AST. At the national level, data should be validated using a similar approach and corrections may need to be requested through communications with participating surveillance sites.

9.5.1 Removal of duplicate results

Individual patients are often sampled repeatedly for diagnostic purposes or to assess the therapeutic response. Patients with infections caused by resistant microorganisms are more likely to be sampled repeatedly. When several cultures are collected during patient management, duplicate findings for the same patient and the same microorganism (more precisely, repeat isolates of the same species, even if the resistance characteristics differ) should be excluded from the source database (de-duplication), keeping the first sample to ensure that data are not biased by repeated measurements.

Before starting the de-duplication process, it is advisable to review variables containing information about the patient and to particularly check whether the database contains patient identifiers or unique counters. If they are missing, a variable with a unique patient identifier or counter should be generated. When there are missing values, a unique identifier could be created, for example, from the patient's personal information data for each missing value.

While the local surveillance sites could apply different de-duplication algorithms, depending on a specific purpose (for example, informing infection prevention and control) and when preparing the hospital antibiograms and local surveillance reports, it is expected that the NCC will take the responsibility of de-duplication according to the national protocol and GLASS recommendations. All consecutive isolates (and negative samples) should be submitted to the NCC, which will remove duplicate results (ideally, with the participation of the surveillance site to build local capacity).

When reporting to GLASS, only one result for each surveillance period (for example, 12 months) should be reported for each patient per surveyed specimen type and surveyed pathogen. For example, if two blood cultures from the same patient yield growth of *E. coli*, only the first isolate should be included in the report; if growth of *E. coli* is detected in one culture and *K. pneumoniae* in the other, both results should be reported. If there is growth of *E. coli* in one blood culture and in one urinary culture from the same patient, both specimen types should be included. The only exception is when on one and the same day, the same pathogen is isolated from both the blood and CSF of a single patient. In this case, only data on the CSF isolate are included in analyses.

If two records for the same patient show the same pathogen in the same specimen type, but the infection origin has changed from hospital to community, both samples should be included. Repeated negative results for the same specimen type in the same patient should also be de-duplicated in the generation of the *SAMPLE* file where the interest is "number of tests performed" and not the results of those tests.

In the example below[13], three patients have several samples taken during the reporting year. Duplicated records to be removed are marked in red:

Sample ID	Patient ID	Specimen	Pathogen	Origin
27	A	BLOOD	ESCCOL	HO
~~244~~	~~A~~	~~BLOOD~~	~~BLOOD~~	~~HO~~
369	B	BLOOD	KLEPNE	HO
~~394~~	~~B~~	~~BLOOD~~	~~NEGATIVE~~	~~HO~~
~~438~~	~~B~~	~~BLOOD~~	~~NEGATIVE~~	~~HO~~
626	A	BLOOD	ESCCOL	CO
627	C	BLOOD	NEGATIVE	HO
~~760~~	~~A~~	~~BLOOD~~	~~ESCCOL~~	~~HO~~
792	B	URINE	NEGATIVE	HO
801	A	URINE	KLEPNE	HO
~~805~~	~~A~~	~~URINE~~	~~KLEPNE~~	~~HO~~
~~900~~	~~C~~	~~BLOOD~~	~~NEGATIVE~~	~~HO~~

De-duplication promotes standardization and comparison of the data at the local, national, regional and global levels.

9.5.2 Data encryption

WHO is committed to data protection and privacy for patients and healthcare facilities. For that reason, the patient identification (ID) number and the sample ID available at the local surveillance sites and NCC should be encrypted in accordance with country legislation before the data are shared with GLASS. Encryption of the patient ID can be accomplished using the standard function available in WHONET or using other encryption tools available. At the national level, laboratory and hospital codes should be generated. The hospital and laboratory names will only be available at the national level and will not be shared with GLASS.

9.5.3 Data anonymization

Laboratory data may contain personal information. It is important that all information that may lead to the identification of a patient is removed before data are sent to a national or international surveillance network. Examples of identifying information are names, birth dates, home addresses, and national identifiers, such as social security numbers. Such information should not be used as a patient identifier. The unique identifier should not be traceable to the patient and has to be encrypted if the original one is an identifying element.

9.5.4 Grouping antimicrobials

Grouping of antimicrobials is needed when aggregated data are reported to GLASS (see Section 7.2.1). The priority sequence R → I → S is used to classify AST results in a pathogen. When combining the results for the antimicrobial representing the group or class, the outcome is based on the most resistant result and so it is important to note that the resulting data may not indicate resistance to all antimicrobials in the group. For example, if a pathogen's susceptibility to imipenem is "I" and susceptibility to meropenem is "R", then the susceptibility to carbapenems is set to "R". Of note, this approach should be applied with caution as such an extrapolation could lead to over-reporting of resistance for some classes where different resistance mechanisms are present, for example, aminoglycosides or fluoroquinolones.

9.5.5 Data aggregation and submission to GLASS

9.5.5.1 Submission of aggregated data

The NCC is responsible for preparing the aggregated GLASS RIS and SAMPLE datasets from data collected at the surveillance sites. The first step for the data manager at the NCC is to combine the datasets from all local surveillance sites into one dataset. The resulting data should be aggregated according to specifications detailed in Annexes 1 and 2. The WHONET software has automated export functions that include the generation

13 This is a simplified view of the database, not all variables that should be part of the source database are shown here

of the *RIS* and *SAMPLE* files. If relevant microbiology test results are stored within a laboratory information system (LIS), the data can be imported into WHONET using the BacLink data import utility (bundled with WHONET); which can then produce the *RIS* and *SAMPLE* datasets using the automated export functions. When the *RIS* and *SAMPLE* files are generated, they can be uploaded to the GLASS IT platform *(68)* as described in the *Guide to use of the GLASS IT platform*[14].

9.5.5.2 Submission of individual level data

Preparation of the individual level GLASS dataset also starts with combining the datasets from all local surveillance sites into one national dataset. The resulting data should be exported in the GLASS individual file format. It is important to ensure that the data are properly anonymized and encrypted before submission. The WHONET software has automated export function that include generation of the GLASS individual dataset compatible with the datasets collected by the WHO regional networks. When the GLASS individual level dataset is generated, it can be uploaded via the individual data module in the GLASS IT platform as described in the *Guide to the use of the GLASS IT platform.*

9.5.6 Global and regional management of GLASS-AMR data

GLASS has developed an IT platform for global data sharing on AMR. Launched in 2016, the platform is hosted on a WHO server and serves as a common environment for standardized data submission, validation, analysis, reporting and data sharing with countries and WHO regional and country offices.

The GLASS-IT platform is a secure web-based platform with user-specific roles and access rights. The platform accepts data in a number of formats, thus allowing for flexibility and tailored approaches to the needs of individual countries and WHO teams from regional and country offices. This shared ownership of the global AMR data repository allows collaborative work with countries, and the generation of different analyses and reports at the global, regional and country levels.

All GLASS databases are accessed with unique authentication and rights management processes. Users of the GLASS-IT platform can upload, manage and submit data, access upload history, access and download previously submitted data and generate customised data reports. Users can also access statistical information and dashboards based on data provided. All databases have common data workflows (enrolment, data upload, data validation, import, and report publication).

14User guide to the GLASS IT platform: submission and analysis of AMR data (tentative title, work in progress)

10 Analysis and reporting of data

The GLASS global report on AMR surveillance is produced every year and includes progress in establishing surveillance capacity, quality and reporting at national and regional levels. Detailed data showing the progress of countries and AMR data are published and made available on the GLASS *(69)* and WHO Global Health Observatory *(70)* websites.

Currently GLASS reports both the **proportion of drug-resistant infections** among all patients with a microbiologically-confirmed infection for each specimen-pathogen-antibiotic combination; and **frequency of infection caused by resistant pathogens** among the population of patients who sought medical care and from whom samples have been collected for microbiological testing in the reporting period.

In its next implementation phase GLASS is collecting a larger amount of information, particularly through the individual-level module and national AMR prevalence surveys. Various measures of the occurrence of AMR in defined populations can be generated, depending on the information available on the events (numerator) and the group of the target population (denominator). Stratification and risk factor analysis can help associate AMR with a group of patients or clinical drivers. New analytical approaches will be developed according to the availability and nature of collected data.

10.1 Key AMR metrics for global reporting

Proportion of drug-resistance. For each specimen type, pathogen and antimicrobial drug under surveillance, the proportions of patients with growth of resistant strains are calculated using the following formula and presented graphically:

$$\frac{\text{Number of patients, per specimen type, with infection by pathogen}_X \text{ resistant to antibiotic}_Y \text{ under surveillance}}{\text{Total number of patients,per specimen type, with infection by pathogen}_X \text{ susceptible,I,and resistant to antibiotic}_Y \text{ under surveillance}} * 100\%$$

Note that due to selective testing, although the infected population for a specific pathogen under surveillance does not change, the denominator will change based on the antibiotic under surveillance, as the actual number of patients comprising the denominator is based on the availability of AST results for that antibiotic.

Example:

Number of patients with bloodstream infections caused by E. coli resistant to cefotaxime / number of patients with bloodstream infection caused by E. coli with AST results (susceptible, I, resistant) for cefotaxime.

Frequency of infections and drug-resistant infections. For countries that submitted sample-based data, a further analysis is performed. It is important to note that as countries are asked to provide only clinically significant results, positive cultures reported are considered to be a proxy for infection. In addition, data de-duplication only allows new cases to be reported. Thus, the frequency of infection with pathogens under surveillance and the frequency of infection with pathogens resistant to specific antibiotics are calculated for the tested population, defined as the total number of symptomatic patients that sought medical care and from which samples of different specimen types where taken.

For each specimen type, infection origin and pathogen, rates of patients with new infections are calculated per 100 000 tested patients using the following formula and presented graphically:

$$\frac{\text{Number of patients, per specimen type, with infection by pathogen}_X \text{ under surveillance}}{\text{Population tested during the reporting period per specimen type and infection origin}} * 100000$$

Example:

Number of patients with bloodstream infection of community origin caused by E. coli / number of patients with suspected infection of community origin from which a blood sample was taken

Subsequently, for each specimen type, infection origin, pathogen, and antibiotic under surveillance, rates of patients with a new growth of resistant strains, are calculated per 100 000 tested patients, using the following formula and presented graphically:

$$\frac{\text{Number of patients, per specimen type, with infection by pathogen}_x \text{ resistant to antibiotic}_y \text{ under surveillance}}{\text{Population tested during the reporting period per specimen type and infection origin}} * 100000$$

Example:

Number of patients with bloodstream infection of community origin caused by E. coli resistant to cefotaxime / number of patients with suspected infection of community origin from which a blood sample was taken

Note that in this case it is not assumed that the absence of AST results should be interpreted as having a susceptible result, but that patients with no bacterial growth cannot influence the magnitude of resistance patterns in the target population.

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Annex 1 *RIS* dataset variables

Table A1.1. Variables in the *RIS* dataset

Variables in RIS dataset	Type of variable	Example
COUNTRY	Coded value*	*AFG*
REGION	Coded value	*AFR*
YEAR	Coded value	*2015*
SPECIMEN	Coded value	*BLOOD*
PATHOGEN	Coded value	*ACISPP*
GENDER	Coded value	*M*
ORIGIN	Coded value	*HO*
AGE	Coded value	*01>04*
ANTIBIOTIC	Coded value	*AMK*
R	Integer (≥0)	*15*
I	Integer (≥0)	*10*
S	Integer (≥0)	*30*
UNK_NO_AST	Integer (≥0)	*5*
UNK_NO_BP	Integer (≥0)	*0*
BATCHID	Coded value	*DS1*

Abbreviation: HO, hospital.

* Coded values lists for all coded value variables are available in Annex 3.

Variable COUNTRY

COUNTRY is a mandatory coded value variable with three-letter country codes based on ISO 3166-1 (for example, AFG = Afghanistan). The list of country codes with both full and short country (territory) names is available in Annex 3.

Variable REGION

REGION is a mandatory coded value variable with WHO region codes (for example, AFR = African Region).

Variable YEAR

YEAR is a mandatory coded value variable. The value in the RIS file shows the year represented by the data collection, typically using specimen collection date in the source database.

Variable SPECIMEN

SPECIMEN is a mandatory coded value variable. The coded value list for GLASS specimens is available in Annex 3.

Variable PATHOGEN

PATHOGEN is a mandatory coded value variable. The coded value list for GLASS target pathogens is available in Annex 3.

Variable GENDER

GENDER is a mandatory coded value variable. The coded value list is available in Annex 6. Please use the UNK value when the data are not stratified by gender.

Variable ORIGIN

ORIGIN is a mandatory coded value variable. The coded value list is available in Annex 3.

Please note that infections are considered to be of "hospital origin" if patients had been hospitalized for > 2 calendar days when the specimen was taken. This includes the following:

- patient admitted to a health care facility for > 2 calendar days; or
- patient admitted to a health care facility for < 2 calendar days, but transferred from another health care facility where admitted for ≥ 2 calendar days

Infections are considered to be of "community origin" for patients seeking care at an outpatient clinic when the specimen was taken or patients hospitalized for ≤ 2 calendar days when the specimen was taken.

If the data on the patient origin are not entered directly at the surveillance site using the above-mentioned case definitions, the variable ORIGIN could be calculated using the variables with the data on date of admission, date of sample, and patient location type (outpatient vs. inpatient locations).

Please use the UNK value when the data are not stratified by infection origin.

Variable AGE

AGE is a mandatory coded value variable. The coded value list is available in Annex 3. Please note that the sign "<" is used in the AGEGROUP codes instead of the sign "-": this is to avoid re-formatting issues in Microsoft Excel. Please use the UNK value when the data are not stratified by age.

Variable ANTIBIOTIC

ANTIBIOTIC is a mandatory coded value variable. The coded value list is available in Annex 3 and includes codes for individual antimicrobials.

Variable R

R is a mandatory integer (≥0) variable representing the number of isolates resistant to a specific antibiotic. This includes AST results interpreted as resistant ("R"), according to EUCAST *(71)* or CLSI *(62)* (and including a nonsusceptible [NS] category according to CLSI) definitions of susceptibility categories.

Variable I

I is a mandatory integer (≥0) variable representing the number of isolates with AST results interpreted as susceptible, increased exposure according to EUCAST or intermediate (including susceptible-dose dependent) according to CLSI.

Variable S

S is a mandatory integer (≥0) variable representing the number of isolates with AST results interpreted as susceptible, standard dosing regimen, according to EUCAST or susceptible according to CLSI.

Variable UNK_NO_AST

UNK_NO_AST is a mandatory integer (≥0) variable representing the number of isolates with AST results not reported (not performed) for a specific antibiotic.

Variable UNK_NO_BP

UNK_NO_BP is a mandatory integer (≥0) variable representing the number of isolates with AST performed but no interpretation of results available for a specific antibiotic.

Both UNK_NO_AST and UNK_NO_BP are very important for assessing selection bias and countries are encouraged to always report missing AST results. When the data show a high percentage of unknown AST results for specific antimicrobials, the level of uncertainty on the generated AMR rates could be very high[1].

Variable BATCH_ID

BATCH_ID is a mandatory coded value variable. It is introduced to distinguish subsets of national aggregated data provided by a country where it is not possible to aggregate national data in the same way for some reason, or when dividing the national dataset has an important added value. For example, this may be needed if the country has different surveillance systems or there is a

1 Currently GLASS applies 30% unknown AST results cut-off value when reporting different outcomes. This value was selected as giving a reasonable balance in terms of results inclusion and proportion of isolates with data available

need to report data from different parts of the country separately. For example, BATCH_ID may also be needed if the sample statistics (needed for generating a SAMPLE file) are missing for a large part of the country.

Table A1.2. Using BATCHID: an example of country A

Data set	RIS file	SAMPLE file	Comments
Dataset 1 from surveillance sites A, B, F (BATCHID=DS1)	Available	Available	Data will be used to calculate both proportions and AMR rates per 100 000 sampled patients for dataset 1
Dataset 2 from surveillance sites C, D, E, G (BATCHID=DS2)	Available	Not available	Data will be used in reports displaying proportions only (%) for dataset 2
National dataset (total)	Dataset 1 + Dataset 2	ND*	Data will be used in reports displaying proportions only (%) for country A

* ND = no data

Countries are free to choose up to five datasets (dataset 1, dataset 2, dataset 3, dataset 4, and dataset 5). The dataset 1 (DS1) value is used by definition when data are reported as a single set.

Annex 2. *SAMPLE* dataset variables

The SAMPLE dataset variables are shown in the Table 8 below:

Table A2.1. Variables in the SAMPLE dataset

Variables in SAMPLE dataset	Type of variable	Example
COUNTRY	Coded value	*AFG*
YEAR	Coded value	*2015*
SPECIMEN	Coded value	*BLOOD*
GENDER	Coded value	*M*
ORIGIN	Coded value	*HO*
AGEGROUP	Coded value	*01>04*
NUMSAMPLEDPATIENTS	Integer (≥0)	*1000*
NUMINFECTED	Integer (≥0)	*1000*
BATCHID	Coded value	*DS1*

Abbreviation: HO, hospital

The variables COUNTRY, YEAR, SPECIMEN, GENDER, ORIGIN, AGEGROUP, and BATCHID in the SAMPLE file have the same specifications as those in the RIS file and the same coded values (see Annex 3. Coded values for variables collected with national aggregated data).

Variable NUMSAMPLEDPATIENTS

NUMSAMPLEDPATIENTS is a mandatory integer variable. It represents the number of patients with samples collected for bacteriological testing and includes all positive samples (both isolates of GLASS target pathogens and other bacteria) and negative (no growth) samples.

Variable NUMINFECTED

NUMINFECTED is a mandatory integer variable. It represents the number of patients with samples positive for GLASS target pathogens.

For the BLOOD specimens, all blood samples taken for bacteriological testing are included. All URINE specimens should be counted, independently of the type of collection. For STOOL specimens, all faecal samples from patients collected for bacteriological testing should be counted, excluding samples sent specifically for the detection of *Clostridium difficile* and samples taken to detect viruses and parasites.

Annex 3. Coded values for variables collected with national aggregated data

Variable ***COUNTRY, TERRITORY*** and ***AREA***

Coded value	Label	Country (territory, area)
AFG	Afghanistan	Islamic Republic of Afghanistan
ALB	Albania	Republic of Albania
DZA	Algeria	People's Democratic Republic of Algeria
AND	Andorra	Principality of Andorra
AGO	Angola	Republic of Angola
ATG	Antigua and Barbuda	Antigua and Barbuda
ARG	Argentina	Argentine Republic
ARM	Armenia	Republic of Armenia
AUS	Australia	Australia
AUT	Austria	Republic of Austria
AZE	Azerbaijan	Republic of Azerbaijan
BHS	Bahamas	Commonwealth of the Bahamas
BHR	Bahrain	Kingdom of Bahrain
BGD	Bangladesh	People's Republic of Bangladesh
BRB	Barbados	Barbados
BLR	Belarus	Republic of Belarus
BEL	Belgium	Kingdom of Belgium
BLZ	Belize	Belize
BEN	Benin	Republic of Benin
BTN	Bhutan	Kingdom of Bhutan
BOL	Bolivia (Plurinational State of)	Plurinational State of Bolivia
BIH	Bosnia and Herzegovina	Bosnia and Herzegovina
BWA	Botswana	Republic of Botswana
BRA	Brazil	Federative Republic of Brazil
BRN	Brunei Darussalam	Brunei Darussalam

Variable ***COUNTRY, TERRITORY*** and ***AREA***

Coded value	Label	Country (territory, area)
BGR	Bulgaria	Republic of Bulgaria
BFA	Burkina Faso	Burkina Faso
BDI	Burundi	Republic of Burundi
CPV	Cabo Verde	Republic of Cabo Verde
KHM	Cambodia	Kingdom of Cambodia
CMR	Cameroon	Republic of Cameroon
CAN	Canada	Canada
CAF	Central African Republic	Central African Republic
TCD	Chad	Republic of Chad
CHL	Chile	Republic of Chile
CHN	China	People's Republic of China
COL	Colombia	Republic of Colombia
COM	Comoros	Union of the Comoros
COG	Congo	Republic of the Congo
COK	Cook Islands	Cook Islands
CRI	Costa Rica	Republic of Costa Rica
CIV	Côte d'Ivoire	Republic of Côte d'Ivoire
HRV	Croatia	Republic of Croatia
CUB	Cuba	Republic of Cuba
CYP	Cyprus	Republic of Cyprus
CZE	Czech Republic	Czech Republic
PRK	Democratic People's Republic of Korea	Democratic People's Republic of Korea
COD	Democratic Republic of the Congo	Democratic Republic of the Congo
DNK	Denmark	Kingdom of Denmark
DJI	Djibouti	Republic of Djibouti
DMA	Dominica	Commonwealth of Dominica
DOM	Dominican Republic	Dominican Republic
ECU	Ecuador	Republic of Ecuador
EGY	Egypt	Arab Republic of Egypt
SLV	El Salvador	Republic of El Salvador
GNQ	Equatorial Guinea	Republic of Equatorial Guinea
ERI	Eritrea	State of Eritrea
EST	Estonia	Republic of Estonia

Variable ***COUNTRY, TERRITORY*** and ***AREA***

Coded value	Label	Country (territory, area)
SWZ	Eswatini	Kingdom of Eswatini
ETH	Ethiopia	Federal Democratic Republic of Ethiopia
FJI	Fiji	Republic of Fiji
FIN	Finland	Republic of Finland
FRA	France	French Republic
GAB	Gabon	Gabonese Republic
GMB	Gambia	Islamic Republic of the Gambia
GEO	Georgia	Georgia
DEU	Germany	Federal Republic of Germany
GHA	Ghana	Republic of Ghana
GRC	Greece	Hellenic Republic
GRD	Grenada	Grenada
GTM	Guatemala	Republic of Guatemala
GIN	Guinea	Republic of Guinea
GNB	Guinea-Bissau	Republic of Guinea-Bissau
GUY	Guyana	Republic of Guyana
HTI	Haiti	Republic of Haiti
HND	Honduras	Republic of Honduras
HUN	Hungary	Hungary
ISL	Iceland	Republic of Iceland
IND	India	Republic of India
IDN	Indonesia	Republic of Indonesia
IRN	Iran (Islamic Republic)	Islamic Republic of Iran
IRQ	Iraq	Republic of Iraq
IRL	Ireland	Ireland
ISR	Israel	State of Israel
ITA	Italy	Republic of Italy
JAM	Jamaica	Jamaica
JPN	Japan	Japan
JOR	Jordan	Hashemite Kingdom of Jordan
KAZ	Kazakhstan	Republic of Kazakhstan
KEN	Kenya	Republic of Kenya
KIR	Kiribati	Republic of Kiribati

Variable ***COUNTRY, TERRITORY*** and ***AREA***

Coded value	Label	Country (territory, area)
KWT	Kuwait	State of Kuwait
KGZ	Kyrgyzstan	Kyrgyz Republic
LAO	Lao People's Democratic Republic	Lao People's Democratic Republic
LVA	Latvia	Republic of Latvia
LBN	Lebanon	Lebanese Republic
LSO	Lesotho	Kingdom of Lesotho
LBR	Liberia	Republic of Liberia
LBY	Libya	Libya
LTU	Lithuania	Republic of Lithuania
LUX	Luxembourg	Grand Duchy of Luxembourg
MDG	Madagascar	Republic of Madagascar
MWI	Malawi	Republic of Malawi
MYS	Malaysia	Malaysia
MDV	Maldives	Republic of Maldives
MLI	Mali	Republic of Mali
MLT	Malta	Republic of Malta
MHL	Marshall Islands	Republic of the Marshall Islands
MRT	Mauritania	Islamic Republic of Mauritania
MUS	Mauritius	Republic of Mauritius
MEX	Mexico	United Mexican States
FSM	Micronesia (Federated States of)	Federated States of Micronesia
MCO	Monaco	Principality of Monaco
MNG	Mongolia	Mongolia
MNE	Montenegro	Montenegro
MAR	Morocco	Kingdom of Morocco
MOZ	Mozambique	Republic of Mozambique
MMR	Myanmar	Republic of the Union of Myanmar
NAM	Namibia	Republic of Namibia
NRU	Nauru	Republic of Nauru
NPL	Nepal	Federal Democratic Republic of Nepal
NLD	Netherlands (Kingdom of the)	Kingdom of the Netherlands
NZL	New Zealand	New Zealand
NIC	Nicaragua	Republic of Nicaragua

Variable ***COUNTRY, TERRITORY*** and ***AREA***

Coded value	Label	Country (territory, area)
NER	Niger	Republic of the Niger
NGA	Nigeria	Federal Republic of Nigeria
NIU	Niue	Republic of Niue
MKD	North Macedonia	North Macedonia
NOR	Norway	Kingdom of Norway
OMN	Oman	Sultanate of Oman
PAK	Pakistan	Islamic Republic of Pakistan
PLW	Palau	Republic of Palau
PSE	Palestine	occupied Palestinian territory
PAN	Panama	Republic of Panama
PNG	Papua New Guinea	Independent State of Papua New Guinea
PRY	Paraguay	Republic of Paraguay
PER	Peru	Republic of Peru
PHL	Philippines	Republic of the Philippines
POL	Poland	Republic of Poland
PRT	Portugal	Portuguese Republic
QAT	Qatar	State of Qatar
KOR	Republic of Korea	Republic of Korea
MDA	Republic of Moldova	Republic of Moldova
ROU	Romania	Romania
RUS	Russian Federation	Russian Federation
RWA	Rwanda	Republic of Rwanda
KNA	Saint Kitts and Nevis	Saint Kitts and Nevis
LCA	Saint Lucia	Saint Lucia
VCT	Saint Vincent and the Grenadines	Saint Vincent and the Grenadines
WSM	Samoa	Independent State of Samoa
SMR	San Marino	Republic of San Marino
STP	Sao Tome and Principe	Democratic Republic of Sao Tome and Principe
SAU	Saudi Arabia	Kingdom of Saudi Arabia
SEN	Senegal	Republic of Senegal
SRB	Serbia	Republic of Serbia
SYC	Seychelles	Republic of Seychelles
SLE	Sierra Leone	Republic of Sierra Leone

Variable ***COUNTRY, TERRITORY*** and ***AREA***

Coded value	Label	Country (territory, area)
SGP	Singapore	Republic of Singapore
SVK	Slovakia	Slovak Republic
SVN	Slovenia	Republic of Slovenia
SLB	Solomon Islands	Solomon Islands
SOM	Somalia	Federal Republic of Somalia
ZAF	South Africa	Republic of South Africa
SSD	South Sudan	Republic of South Sudan
ESP	Spain	Kingdom of Spain
LKA	Sri Lanka	Democratic Socialist Republic of Sri Lanka
SDN	Sudan	Republic of the Sudan
SUR	Suriname	Republic of Suriname
SWE	Sweden	Kingdom of Sweden
CHE	Switzerland	Swiss Confederation
SYR	Syrian Arab Republic	Syrian Arab Republic
TJK	Tajikistan	Republic of Tajikistan
THA	Thailand	Kingdom of Thailand
TLS	Timor-Leste	Democratic Republic of Timor-Leste
TGO	Togo	Togolese Republic
TON	Tonga	Kingdom of Tonga
TTO	Trinidad and Tobago	Republic of Trinidad and Tobago
TUN	Tunisia	Republic of Tunisia
TUR	Türkiye	Republic of Türkiye
TKM	Turkmenistan	Turkmenistan
TUV	Tuvalu	Tuvalu
UGA	Uganda	Republic of Uganda
UKR	Ukraine	Ukraine
ARE	United Arab Emirates	United Arab Emirates
GBR	United Kingdom of Great Britain and Northern Ireland	United Kingdom of Great Britain and Northern Ireland
TZA	United Republic of Tanzania	United Republic of Tanzania
USA	United States of America	United States of America
URY	Uruguay	Eastern Republic of Uruguay
UZB	Uzbekistan	Republic of Uzbekistan

Variable ***COUNTRY, TERRITORY*** and ***AREA***

Coded value	Label	Country (territory, area)
VUT	Vanuatu	Republic of Vanuatu
VEN	Venezuela (Bolivarian Republic of)	Bolivarian Republic of Venezuela
VNM	Viet Nam	Socialist Republic of Viet Nam
YEM	Yemen	Republic of Yemen
ZMB	Zambia	Republic of Zambia
ZWE	Zimbabwe	Republic of Zimbabwe
KOS	Kosovo[2]	Kosovo

Variable ***BATCH_ID***

Coded value	Batch ID	Label
DS1	Data Set 1	Data Set 1
DS2	Data Set 2	Data Set 2
DS3	Data Set 3	Data Set 3
DS4	Data Set 4	Data Set 4
DS5	Data Set 5	Data Set 5
EGASP	EGASP	EGASP

Variable ***SPECIMEN***

Coded value	Specimen	Label
BLOOD	Blood	BLOOD
CSF	Cerebrospinal fluid	CSF
URINE	Urine	URINE
STOOL	Stool	STOOL
LOWRESP	Lower respiratory tract	LOWRESP
UROGENITAL	Urethral and cervical swabs	UROGENITAL
ANORECTAL	Anorectal swabs	ANORECTAL

2 All references to Kosovo should be understood to be in the context of the United Nations Security Council resolution 1244 (1999)

Variable ***SPECIMEN***

Coded value	Specimen	Label
PHARYNGEAL	Pharyngeal swabs	PHARYNGEAL

Variable ***PATHOGEN***

Coded value	Specimen	Label
ACISPP	*Acinetobacter* spp.	*Acinetobacter* spp.
ESCCOL	*Escherichia coli*	*Escherichia coli*
HAEINF	*Haemophilus influenzae*	*Haemophilus influenzae*
KLEPNE	*Klebsiella pneumoniae*	*Klebsiella pneumoniae*
NEIGON	*Neisseria gonorrhoeae*	*Neisseria gonorrhoeae*
NEIMEN	*Neisseria meningitidis*	*Neisseria meningitidis*
PSEAER	*Pseudomonas aeruginosa*	*Pseudomonas aeruginosa*
SALSPP	*Salmonella* spp.	*Salmonella* spp.
SALPAR	*Salmonella enterica* serovar Paratyphi A	*Salmonella enterica* serovar Paratyphi A
SALTYP	*Salmonella enterica* serovar Typhi	*Salmonella enterica* serovar Typhi
SHISPP	*Shigella* spp.	*Shigella* spp.
STAAUR	*Staphylococcus aureus*	*Staphylococcus aureus*
STRPNE	*Streptococcus pneumoniae*	*Streptococcus pneumoniae*

Variable ***GENDER***

Coded value	Gender	Label
M	Male	Male
F	Female	Female
O	Other	Other
UNK	Unknown	Unknown

Variable ***ORIGIN***

Coded value	Origin	Label
HO	Hospital origin	Hospital origin
CO	Community origin	Community origin
UNK	Unknown	Unknown

Variable ***AGE***

Coded value	Age groups (years)	Label
<1	<1	<1
01<04	1-4	1-4
05<14	5-14	5-14
15<24	15-24	15-24
25<34	25-34	25-34
35<44	35-44	35-44
45<54	45-54	45-54
55<64	55-64	55-64
65<74	65-74	65-74
75<84	75-84	75-84
85<	85+	85+
UNK	Unknown	Unknown

Variable ***ANTIBIOTIC*** and ***AB_CLASS***

Coded value	Age groups (years)	Label
AMK	Amikacin	Amikacin
AMC	Amoxicillin-clavulanic acid	Amoxicillin-clavulanic acid
AMP	Ampicillin	Ampicillin
AZM	Azithromycin	Azithromycin
FEP	Cefepime	Cefepime
CFM	Cefixime	Cefixime
CTX	Cefotaxime	Cefotaxime
FOX	Cefoxitin	Cefoxitin
CAZ	Ceftazidime	Ceftazidime
CRO	Ceftriaxone	Ceftriaxone
CXM	Cefuroxime	Cefuroxime
CHL	Chloramphenicol	Chloramphenicol
CIP	Ciprofloxacin	Ciprofloxacin
CLR	Clarithromycin	Clarithromycin
COL	Colistin	Colistin
SXT	Co-trimoxazole	Co-trimoxazole
DOR	Doripenem	Doripenem
ERY	Erythromycin	Erythromycin
ETP	Ertapenem	Ertapenem
GEN	Gentamicin	Gentamicin
IPM	Imipenem	Imipenem
LVX	Levofloxacin	Levofloxacin
MEC	Mecillinam	Mecillinam
MEM	Meropenem	Meropenem
MNO	Minocycline	Minocycline
NIT	Nitrofurantoin	Nitrofurantoin
OXA	Oxacillin	Oxacillin
PEN	Penicillin G	Penicillin G
TZP	Piperacillin/tazobactam	Piperacillin/tazobactam
RIF	Rifampicin	Rifampicin
SPT	Spectinomycin	Spectinomycin
TGC	Tigecycline	Tigecycline
TOB	Tobramycin	Tobramycin

ATC Code[3]	Antibiotic sub-group	Label
J01GB	Aminoglycosides	Aminoglycosides
J01BA	Amphenicols	Amphenicols
J01CF	Beta-lactamase resistant penicillins	Beta-lactamase resistant penicillins
J01CE	Beta-lactamase sensitive penicillins	Beta-lactamase sensitive penicillins
J01DH	Carbapenems	Carbapenems
J01CR	Combinations of penicillins, including beta-lactamase inhibitors	Combinations of penicillins, including beta-lactamase inhibitors
J01MA	Fluoroquinolones	Fluoroquinolones
J01DE	Fourth-generation cephalosporins	Fourth-generation cephalosporins
J01FA	Macrolides	Macrolides
J01XE	Nitrofuran derivatives	Nitrofuran derivatives
J01XX	Other antibacterials	Other antibacterials
J01CA	Penicillins with extended spectrum	Penicillins with extended spectrum
J01XB	Polymyxins	Polymyxins
J01DC	Second-generation cephalosporines	Second-generation cephalosporines
J01EE	Sulfonamides and trimethoprim	Sulfonamides and trimethoprim
J01AA	Tetracyclines	Tetracyclines
J01DD	Third-generation cephalosporins	Third-generation cephalosporins

3 ATC/DDD Index 2020 (https://www.whocc.no/)

Annex 4. Coded values for variables collected with individual data

Variable ***HospitalUnitType***

Coded value	Department	Label
INTMED	Internal medicine	Internal medicine
PEDS	Paediatrics/neonatal	Paediatrics/neonatal
PEDSICU	Paediatrics/neonatal ICU	Paediatrics/neonatal ICU
SURG	Surgery	Surgery
ONCOL	Haematology/oncology	Haematology/oncology
OBGYN	Obstetrics/gynaecology	Obstetrics/gynaecology
ICU	ICU = intensive care unit	ICU = intensive care unit
ED	Emergency department	Emergency Department
URO	Urology	Urology
INFECT	Infectious disease	Infectious disease
O	Other	Other
UNK	Unknown	Unknown

Annex 5. Types of care

Acute care involves short-term treatment for a severe injury or episode of illness, an urgent medical condition, or during recovery from surgery. Acute care may be delivered in hospitals or outpatient clinics not linked to hospitals.

Long-term care is delivered to patients who need assistance to function in their daily lives. Non-acute health care facilities delivering long-term care only include nursing homes, rehabilitation centres or psychiatric centres.

For the purpose of individual-level data submission, health care facilities will be categorized based on the type of care [4], that is, primary, secondary, tertiary and specialized health care facilities (Table A5.1). The choice of stratifying by type of care is important in order to take into account the different types of patients and complexity of procedures that can be associated with an increased risk for AMR.

Table A5.1. Types of care

Type of care	Criteria
Primary care (typically 30-250 beds)	• Few specialties (mainly internal medicine, obstetrics-gynaecology, paediatrics, general surgery or only general practice). • Limited laboratory services are available for general, but not for specialized pathological analysis. • Commonly referred to as a "district hospital", "rural hospital", "community hospital" or "general hospital"
Secondary care (typically 200-800 beds)	• Hospital is highly differentiated by function with 5 to 10 clinical specialities, such as haematology, oncology, nephrology, intensive care unit (ICU). • Takes some referrals from other (primary) hospitals. • May have teaching activities. • Commonly referred to as a "regional hospital", "provincial (county) hospital" or "general hospital"
Tertiary care (typically 300-1500 beds)	• Highly specialized staff and technical equipment (ICU, haematology, transplantation, cardio-thoracic surgery, neurosurgery). • Clinical services are highly differentiated by function. • Specialized imaging units. • Regularly takes referrals from other (primary and secondary) hospitals. • Often a university hospital or associated with a university. • Commonly referred to as a "national hospital", "central hospital" or "academic or university hospital"

When a hospital has facilities with different levels of care, then the highest hospital category should be reported. For example, if one facility of the hospital belongs to the primary level and another facility belongs to the tertiary level, then the reported category should be the tertiary hospital.

4 WHO methodology for point prevalence survey on antibiotic use in hospitals, version 1.1. Geneva: World Health Organization; 2018 (https://apps.who.int/iris/handle/10665/280063)

Annex 6. Implementation questionnaire[5]

WHO Region	
Country	
Year	

1 Has a National Coordination Centre (NCC)* been established?

- Yes, with a mandate and terms of reference in line with the GLASS manual
- In progress
- No
- Unknown

*The National Coordinating Centre (NCC) is an institution appointed by national authorities to oversee the development and functioning of the national AMR surveillance system and reporting to GLASS. It is composed of a multi-disciplinary team of infectious disease clinicians, microbiologists, epidemiologists, and data managers. The NCC is usually, but not always, a public health institution such as a public health institute or a government (ministry of health) department.

2 Have one or more National Reference Laboratory(s) (NRL)* been designated to support national AMR surveillance in humans?

- Yes
- No
- Unknown

*A National Refence Laboratory (NRL) is a specialist laboratory with expertise in methods for characterizing AMR pathogens and providing support to the national AMR surveillance system (some countries prefer having a network of several reference laboratories covering specific pathogens). The NRL promotes and facilitates good laboratory practice in the country, as well as the harmonization of methods and standards used in the national AMR surveillance system.

3 Does the NRL participate in an external quality assurance* (EQA) scheme?

- Yes
- No
- Unknown

*Quality assurance is practice that encompasses all procedures and activities for ensuring that a specified quality of laboratory service is achieved and maintained. Quality assurance is composed of internal quality control (IQC) (within the laboratory) and external quality assurance (EQA) which includes other laboratories or an EQA provider. An example of IQC is using ATCC positive and negative controls of bacteria for identification and antibiotic susceptibility testing in the laboratory. Alternatively, an example of EQA is proficiency testing in which the laboratory participates in the identification and antibiotic susceptibility of a known isolate sent by an EQA provider.

4 Which antimicrobial susceptibility testing (AST) standards are applied in your country?

- CLSI (Clinical and Laboratory Standards Institute)
- EUCAST (European Committee on Antimicrobial Susceptibility Testing)
- Other
- Unknown

5 Any further reference to ”country” and ”national” in this questionnaire should be understood to refer countries, territories and areas as well as national and local institutions, data and information. Use of the terms ”country” and ”national” does not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities.

5 National infrastructure and utilization (leave blank if unknown)

5.1 Please provide the number of total acute care* healthcare facilities in your country for the year of collection of reported AMR data

5.2 Among (5.1), provide the total count of hospitals

5.3 Among (5.1), provide the total count of outpatient consultations**

5.4 Among (5.1), provide the total count of inpatient*** admissions

5.5 Among (5.1), provide the total count of inpatient days of care****

*Acute care involves short-term treatment for a severe injury or episode of illness, an urgent medical condition, or during recovery from surgery. Acute care may be delivered in hospitals or outpatient clinics not linked to hospitals.
**This is the total number of patients that go to a healthcare facility for diagnosis or treatment, but who do not require to be admitted for overnight stay. Count the total number of consultations including revisits.
*** Inpatient: a person who is formally admitted to a healthcare facility and who is discharged after one or more days
****Corresponds to the sum of each daily inpatient census for the year. To arrive at this total, for any given healthcare facility, each daily census for the 365 days in the year is added together. The count assumes that the number of patients on the inpatient wards (excluding outpatients) is recorded at the same time each day. A different way of calculating the inpatients days of care is to calculate the number of bed-days for each admitted inpatient (i.e., adding up the length of stay for each inpatient admitted in 2020). A bed-day corresponds to that in which a person admitted as an inpatient is confined to a bed for an overnight stay. The number of bed-days is counted as the date of discharge minus the date of admission (for example, a patient admitted on the 25th and discharged on the 26th should be counted as 1 day).

6 Are you submitting AMR data to GLASS during the current data call?

Yes*

No**

* If "Yes", you will be automatically directed to question 7
**If "No", you will be automatically directed to question 9

7 National infrastructure contributing to GLASS (leave blank if unknown)

7.1 Please provide the number of total acute care healthcare facilities in your country that reported at least one result to GLASS in the previous year of data collection

7.2 Among (7.1), provide the count of hospitals

7.3 Among (7.2), provide the total count of outpatient consultations

7.4 Among (7.1), provide the total of count inpatient admissions

7.5 Among (7.1), provide the total count of inpatient days of care

8 National diagnostic capacity contributing to GLASS (leave blank if unknown)

8.1 Please provide the total number of laboratories that reported at least one result to GLASS in the year of data collection

8.2 Among (8.1), provide the number of laboratories that participate in a national EQA programme

9 Could you please provide a brief introduction to the current country AMR surveillance structure and/or activities (max length 1500 characters)

Annex 7. Molecular indicators

GLASS target pathogens	Mechanisms of resistance	Molecular targets
Acinetobacter spp. *Pseudomonas aeruginosa*	Carbapenem resistance	NDM, OXA, VIM, IMP, GES, KPC
	Colistin resistance	mcr 1-10
Escherichia coli *Klebsiella pneumoniae* *Salmonella spp.* *Shigella spp.*	Extended spectrum beta-lactamases	CTX-M, TEM, SHV
	Carbapenem resistance	NDM, OXA, VIM, IMP, GES, KPC
	Colistin resistance	mcr 1-10
Staphylococcus aureus	Methicillin resistance	mecA/mecC
	Linezolid resistance	cfr

World Health Organization
20 avenue Appia
1211 Geneva 27
Switzerland

https://www.who.int/health-topics/antimicrobial-resistance