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World Health
Organization

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Abbreviations and acronyms

AMR	antimicrobial resistance
AMC	antimicrobial consumption
AMU	antimicrobial use
AST	antimicrobial susceptibility test/testing
BSI/s	bloodstream infection/s
CLSI	Clinical and Laboratory Standards Institute
EUCAST	European Committee on Antimicrobial Susceptibility Testing
GLASS	Global Antimicrobial Resistance and Use Surveillance System
HIV	human immunodeficiency virus
LMICs	low- and middle-income countries
SDG	Sustainable Development Goal/s
WHO	World Health Organization

1. Introduction

Antimicrobial resistance (AMR) is among the top 10 global health threats (1). High rates of resistant infections have been documented in all World Health Organization (WHO) regions and for a broad range of microorganisms (2). In 2019, an estimated 4.95 million deaths were associated with bacterial AMR, including 1.27 million deaths attributable to bacterial AMR (2). Although the overuse or misuse of antibiotics are primary drivers of the emergence and maintenance of AMR, other multiple interconnected factors contribute to its prevalence. Higher AMR rates have been documented in several low- and middle-income countries (LMICs) compared to high-income countries, despite a lower per-person consumption of antibiotics in the former (3, 4). Alert to this crisis, the Sixty-eighth World Health Assembly held in May 2015 adopted a global action plan endorsing the urgent need for strengthening the knowledge and evidence base of AMR through surveillance and research in order to tackle this threat (5).

To generate high-quality evidence of the magnitude (prevalence and incidence), distribution (for example, across geographical areas and populations) and diversity (across pathogens) of AMR globally, a significant investment has been made in improving AMR surveillance through promoting the routine standardized collection, analysis and sharing of global AMR data (6). Launched by the WHO in 2015, the Global Antimicrobial Resistance and Use Surveillance System (GLASS) is the first system that enables a harmonized global reporting of official national AMR and antimicrobial consumption (AMC) data (6, 7). At its core, GLASS comprises surveillance activities built on routinely available data (that is, AMR in priority bacterial human pathogens isolated from clinical specimens and AMC). However, it has continued to rapidly evolve to include focused surveillance activities aimed at generating information for specific purposes (for example, early warning of emerging resistance) and for other pathogens (for example, AMR in *Candida* spp.), as well as targeted studies according to countries' needs to estimate the disease burden of AMR (for example, attributable mortality) and related drivers (for example, antimicrobial use [AMU]) (6, 8). Through collation of routine national AMR surveillance data, GLASS also

informs the new Sustainable Development Goal (SDG) indicator for AMR, which was added in 2020 to the SDG monitoring framework (9, 10). This new indicator (3.d.2)¹ – linked to target 3.d² – is considered a basic building block to help catalyse the establishment of national AMR programmes for AMR monitoring and response in countries. The indicator monitors the proportion of bloodstream infections (BSIs) due to *Escherichia coli* resistant to third-generation cephalosporins and methicillin-resistant *Staphylococcus aureus* (MRSA) (10).



¹ 3.d.2: “Percentage of bloodstream infections due to selected antimicrobial-resistant organisms”.

² 3.d: “Strengthen the capacity of all countries, in particular developing countries, for early warning, risk reduction and management of national and global health risks”.

2. Rationale for national antimicrobial resistance prevalence surveys as a platform for global surveillance

Despite global efforts, considerable gaps remain in our understanding of AMR, including the magnitude of drug-resistant infections worldwide. Developing and sustaining a robust capacity for national surveillance through systematic continuous data collection and analysis from routine clinical activities remains difficult to implement, including where AMR is most prevalent. In addition, this capacity is severely limited in its coverage and representativeness in many countries (Box 1), including those with an adequate infrastructure and others already reporting national surveillance data to GLASS.

Box 1. Undocumented sources of variance that limit the interpretation of AMR data

Multiple undocumented sources of variance severely limit the interpretation of AMR data currently available from routine surveillance, thus making it impossible to differentiate genuine changes in AMR prevalence within and between settings and over time from operational changes. For example, undocumented sources include differences in the composition of healthcare facilities contributing data, number of facilities not reporting data (that is, surveillance coverage), number of eligible patients not being tested (that is, underdiagnosis), the quality of laboratory services, or the number of patients tested for whom results are not reported (that is, underreporting). These factors are closely related to diagnostic access and affordability, as well as clinical and diagnostic practices specific to each setting. A lack of accurate documentation on key risk factors for AMR for individuals with clinical specimens submitted for microbial identification and antimicrobial susceptibility testing (AST), such as prior antibiotic exposure and/or a hospital or community infection origin classification, contribute to these undocumented sources of variance that limit the availability of comparable, interpretable data.

Expediting the availability of robust, generalizable evidence that is comparable between geographical areas is essential to: (1) characterize and track the global scale, impact, distribution and dynamics of AMR; (2) identify emerging and spreading threats; (3) develop measures to prevent and/or mitigate AMR; (4) prioritize settings in need of intervention; (5) evaluate the impact of interventions; (6) assess whether global targets for reductions in AMR and the related burden of disease have been achieved; (7) inform the rationalization of empirical AMU and treatment guidelines; and (8) improve public health decision-making in collaboration with relevant stakeholders.

WHO proposes that national surveys involving the periodic, strategic sampling of a population subset can overcome the paucity of high-quality representative AMR data originating from routine clinical practice in LMICs, where surveillance infrastructures remain sparse. Nationally representative surveys catalysed by WHO through technical guidance and assistance have been successfully implemented since the 1990s to estimate and monitor the national and global prevalence of drug resistance in malaria, tuberculosis and human immunodeficiency virus (HIV) (11-16).

3. Objectives and scope of work

3.1. Objectives and key deliverables

The overarching aim of WHO is to establish nationally representative surveys as a platform for the strategic national and global surveillance of AMR in human bacterial infections in LMICs. In the absence of national surveillance systems of high quality and coverage, national surveys can provide a reliable, direct measurement of the prevalence of AMR. WHO intends to develop a knowledge base for the planning, implementing and reporting of nationally representative surveys to measure the prevalence of AMR, focusing initially on bacterial BSIs in patients seeking acute inpatient care in hospitals.³ Antimicrobial-resistant BSIs are among the most serious life-threatening infectious diseases. Notably, mortality related to bacterial BSIs constitutes 72% of the total health burden of AMR in the European setting (17) and this estimate is likely to be higher in LMICs. BSIs are also the initial focus of other GLASS-targeted studies, thus providing an opportunity for linkage and integration with other activities (for example, AMR attributable mortality, BSIs, etc.).

Box 2. GLASS strategic areas of work to measure progress towards defined milestones and targets for reductions in AMR prevalence

1. Foster the development of robust national AMR and AMU/AMC surveillance systems.
2. Strengthen routine AMR surveillance systems in all countries.
3. Implement national AMR prevalence surveys to remedy the paucity of interpretable data in LMICs.
4. Periodically review the methods used to collect and translate surveillance and survey data into estimates of the magnitude of AMR in human infections.
5. Establish and monitor milestones and targets for reductions in the prevalence and incidence of AMR at global, regional and country levels.

Starting from periodic country-specific surveys, the goal is to progressively build capacity for countries to ultimately establish the strongest possible continuous surveillance systems, based on routine microbial identification and AST of relevant clinical specimens (Box 2).

³ Includes patients investigated and treated for a suspected BSI in the emergency department (emergency room/ accident and emergency department) with delayed transfer to an inpatient ward.

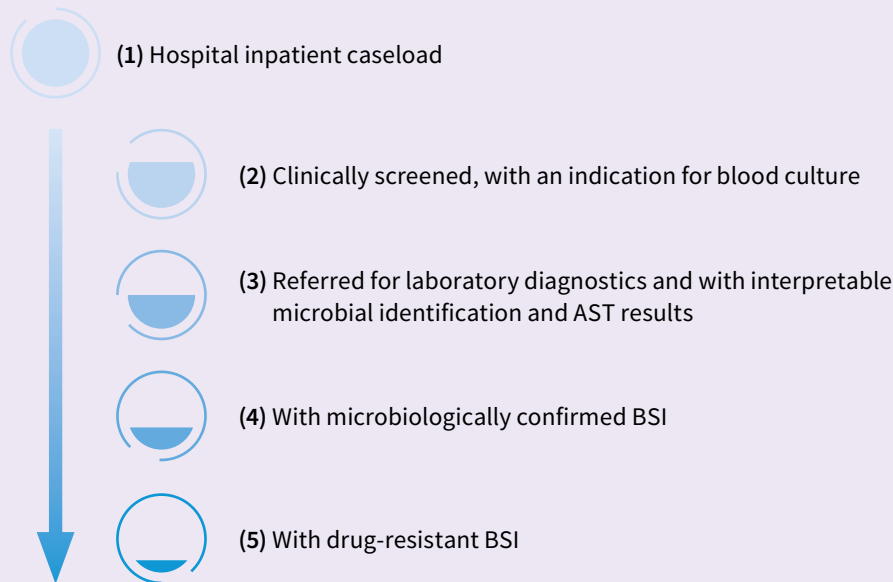
WHO aims to help deliver nationally representative surveys following the best possible ethical and scientific quality standards (18) and applying principles of good clinical practice and good data and record management practices (19, 20). This will ensure that the rights, safety and well-being of survey participants are protected and that evidence-informed national policies can be developed, based on reliable, accurate and complete data (18). Such surveys will provide a knowledge base to accurately inform the estimates of the AMR health burden and targeted mitigation strategies. The specific objectives of this complementary strategy are listed below.

- To estimate the national prevalence of AMR in hospitalized patients with microbiologically confirmed BSI of community or hospital origin, following due consideration of relevant underlying factors (for

example, documentation of antimicrobial therapy).

- To implement a survey approach that takes into account the patient pathway within the healthcare setting when measuring prevalence, strengthens diagnostic stewardship and laboratory practices, and enhances epidemiological capacities, thus minimizing the current bias underlying AMR data from LMICs (Box 3).
- To contribute to strengthening national AMR surveillance capacity, thus improving access to appropriate treatment and care for people with drug-susceptible and drug-resistant BSI.

Box 3. Consideration of the patient pathway within the hospital setting



Selection bias currently underlying routine surveillance data within the hospital setting arises predominantly from unequal access to diagnosis (often an out-of-pocket expense in LMICs), poor diagnostic stewardship, and/or poor microbiology practices. These ultimately result in a misestimation of drug-resistant bacterial infection and a substandard choice of antimicrobial treatment. Consideration of the patient pathway in measuring prevalence involves strengthening procedures to adequately identify and quantify all relevant individuals at each step of the diagnostic process during their healthcare contact. This can inform whether cases are being missed in clinical practice and, if so, which ones, as well as the quality of data reported through routine surveillance and any potential bias, including interventions required to strengthen healthcare service and practices. To design surveys that account for the patient pathway, all patients with plausible BSI must be enrolled in the survey and the inpatient caseload must be recorded from all hospitals participating in the survey. As part of the objectives, surveys will consequently contribute to strengthening clinical, epidemiological and laboratorial diagnostic capacity in the country and will ensure that all people with drug-susceptible and drug-resistant BSIs have timely access to appropriate treatment and care.

The roadmap to achieve the overarching aim involves a sequence of proximate, intermediate, and distal deliverables, as part of the pathway to attain the goal (Table 1).

Table 1. Starting position and key deliverables

Starting position
<ul style="list-style-type: none"> • By default, the current approach to AMR surveillance is based on the assumption that all patients have access to quality diagnostic practices in all settings. However, this assumption is not valid in many LMICs, and strategic decision-making to limit drug-resistant infection in these settings will likely remain poorly informed by evidence for years to come.⁴ • WHO proposes a global surveillance model based on the implementation of periodic nationally representative surveys in LMICs⁵ by building upon well-known survey design methods and standardized criteria scalable to most contexts, which have proven successful as part of WHO global programmes monitoring and tackling drug resistance in malaria, HIV and tuberculosis.
Proximate deliverables
<ul style="list-style-type: none"> • Formation of a multidisciplinary team involving experts from public health agencies, ministries of health, academia, the healthcare community, and WHO. • Initiation of a capacity-building effort, focusing initially on identifying best practice and ethical standards for the implementation of national AMR prevalence surveys in clinically relevant human pathogenic bacteria. • Initiation of a coalition of interested countries and parties/partners who can support the proposed surveillance model by fully leveraging the potential for sharing technical expertise following the implementation of pilot surveys.
Intermediate deliverables
<ul style="list-style-type: none"> • Proof-of-principle implementation of the first nationally representative surveys to estimate the prevalence of AMR in hospitalized patients with microbiologically confirmed BSI. • Co-production of WHO technical guidance for the planning, implementation, analysis, interpretation, dissemination, and use of data from national AMR prevalence surveys.
Distal deliverables
<ul style="list-style-type: none"> • Development of a framework and a roadmap to systematically and strategically scale-up periodic surveys in LMICs by providing a platform for global quality-assured surveillance of AMR that can be expanded to consider infectious syndromes other than BSIs. This will also offer an opportunity for linkage and integration with other activities (for example, environmental sampling) and a channel for the delivery of more detailed studies meeting setting-specific needs (for example, AMR attributable mortality, etc.).

⁴ AMR surveillance data in many LMICs do not provide insight into the cause, type, scale or spread of AMR. Data are often limited to tertiary referral, private hospitals, or research facilities that are often designated as national sentinel sites. These data are likely to be biased towards complex infections, treatment failures and hospital-acquired infections, and/or are too sparse to be confident of their generalizability.

⁵ A summary of WHO's strategic areas of work is given in Box 2 for context.

3.2. Development of technical guidance

The aim of this document is to provide an overview of the rationale for national AMR prevalence surveys and the associated methodological principles before the release of comprehensive technical guidance for the scaling-up of the implementation of surveys.

Lessons learned from the implementation of pilot surveys in 2023 will be shared and discussed in workshops that bring together pilot implementers and international experts tasked with supporting the development of WHO's technical guidance for national AMR prevalence surveys in human infections. The draft guidance will be iteratively revised by building upon the experiences of surveys in pilot countries before publication.

3.3. Broader impact

WHO leads on global health issues by leveraging and shaping development agendas through science-based guidance and technical support at country level. Through its convening power with Member States, particularly ministries of health and regulatory authorities, but also civil society and other global health actors, WHO is in a privileged position to help scale-up periodic surveys for strategic global surveillance of AMR in LMICs and to serve as a platform for the implementation of related activities to inform country action, policies, interventions, and advocacy. Therefore, the pathway to a positive impact is expected to involve addressing distal deliverables in collaboration with a variety of partners through a model of enhanced technical support to countries that also extends to supporting capacity building and coordinating external assistance (Table 1). Quality-assured national data from surveys will feed into GLASS to remedy the paucity and limited representativeness of current data from LMICs.

3.4. Diversity and inclusion

WHO is collaboratively developing technical guidance and driving coordination efforts for the implementation of pilot surveys around the world, but the surveys and resultant data are owned by national authorities implementing these surveys. A survey is expected to be implemented by the ministry of health with support from WHO (country offices, regional offices, and headquarters) and other relevant actors based in the country. A (local) principal investigator should appoint national qualified staff, including an epidemiologist, for the positions of survey coordination, implementation, and monitoring at central and peripheral (hospital) levels. Technical assistance and support to all aspects of the survey planning (for example, protocol development, procurement), implementation, and monitoring should be delivered through the formation of a scientific advisory committee comprising relevant national and international (for example, WHO, supranational laboratory) partners, whilst the principal investigator should lead the planning and implementation operations with the support of country authorities and local technical staff, thus ensuring that experience and capacity are developed and sustained in the country.

4. Where should antimicrobial resistance prevalence surveys be carried out?

Both initially (that is, at the proof-of-principle stage) and in the long term, three major dimensions should be considered when identifying countries where an AMR prevalence survey should be carried out.

First, the added value of survey results. This will be greater in settings meeting the following criteria: where the available routine surveillance data are poorly informative; where no reliable direct measurement of AMR prevalence is available; where there is an indication of poor diagnostic stewardship; and where public health data (for example, such as a high infant mortality rate) are suggestive of added value. Nationwide surveys are also of the greatest relevance in countries where the magnitude and health burden of AMR is expected to be high, based not only on the available literature and data, but also as informed by other indicators, such as the procurement and use of antimicrobials. Subsequent repeat surveys will allow the measurement of trends, which can be used to make inferences about the impact of interventions and inform further actions.

Second, epidemiological criteria. These should also be considered when prioritizing a setting for a national survey over strengthening routine surveillance alone.

For example, the required sample size should be manageable enough for the survey to be feasible in terms of costs and logistics; some preliminary census data should be available to guide the study design; the expected number of plausible and confirmed BSIs and drug-resistant BSIs should be above a reasonable threshold for the survey to be justifiable and cost-effective; and sufficient time should be allowed between repeat surveys for a meaningful comparison of prevalence. An interval of approximately 5 years between surveys is recommended for other global programmes (for example, tuberculosis) measuring the prevalence of drug resistance (13).

Third, survey feasibility criteria. These include some of the epidemiological considerations listed above (for example, required sample size and logistics), plus additional factors required for the successful implementation of a survey (for example, expected participation rate) that ultimately impact on the representativeness, completeness and quality of the data.

5. Prerequisites of a successful survey

For any country meeting the epidemiological criteria for a survey, feasibility aspects must be carefully assessed against implementation prerequisites (21). National surveys should only be implemented in settings where the following feasibility standards are met.

1. Strong commitment and leadership from national authorities, the ministry of health and a core group of professionals, including focal points for AMR surveillance, prevention and control (where available).
2. Identification of a suitable institute, organization or agency to lead and manage the survey and a survey team where all key members have the required availability, qualifications and experience.
3. Sufficient funding available, including for the timely production of survey reports and the effective communication of findings and their implications.
4. Adequate laboratory infrastructure and capacity available or can be established.
5. Possibility of reliable and timely procurement and logistics. For example, a rapid sample referral network is in place or the national transport infrastructure is adequate to allow its implementation.
6. Security in the field for survey teams and participants can be assured.
7. Participation of individuals in the study is likely to be sufficiently high in all survey areas.
8. Strong governance/oversight mechanisms for survey monitoring and related actions can be assured by implementers and funders.
9. Data management can be done according to recommended standards.
10. Adequate external support and technical assistance are available, including from an operational independent national and/or international ethics committee.



6. Methodological principles of national antimicrobial resistance prevalence surveys

6.1. Overview

The main outcome of a cross-sectional survey is to obtain a nationally representative estimate of the prevalence of AMR among hospitalized patients with microbiologically confirmed BSI. This is obtained by following standardized methods that make it possible for the data to be comparable between settings and within settings over time, and according to principles and standards for the ethical implementation of surveillance systems in public health (22). It is therefore critical that the sample of hospitals included in the survey is selected using statistically-meaningful probability sampling methods (for example, random, etc.), irrespective of whether microbiology diagnostic services are available or not on site (Table 2).

Table 2. Key differences between convenience sampling of hospitals, sentinel surveillance and/or the voluntary participation of hospitals, and nationally representative surveys for AMR

Convenience sampling, sentinel, or voluntary participation of hospitals
<ul style="list-style-type: none">• Data <u>potentially</u> representative at the facility (hospital) level only (that is, subject to coverage and methods); provides a self-assessment tool which strengthens and informs individual hospital practices and policies.
National prevalence surveys
<ul style="list-style-type: none">• Data representative at the national level; strengthens and informs national policies. Data are comparable between and within countries and overtime.

A survey will then involve active case finding of patients with suspected BSI, defined through a specific set of clinical signs and symptoms in inpatient wards⁶ from selected hospitals during a pre-defined intake period, typically not exceeding 12 months. The target population should include neonatal, paediatric and adult age groups. Blood samples should be taken from all eligible patients and shipped to the nearest quality assured laboratory for microbiology and AST conducted according to international standards. A minimum set of demographics and clinical information should be obtained for each patient enrolled in the survey.

6.2. Target bacterial species and antimicrobials

Surveys should consider all bacterial pathogens identified from blood cultures, with a particular focus on the bacterial etiologies currently at the core of GLASS activities for global monitoring purposes⁷ given their global prevalence and attributable health burden (7, 23). The list of antimicrobials considered in the survey, following careful consideration of local resources and capacity, should be aligned with national clinical practice and antimicrobial use, as well as the global AMR surveillance objectives of GLASS (23).

Target antimicrobials should broadly include:

- any of the 33 antimicrobials selected for global surveillance of AMR in bacterial pathogens in GLASS (23) *and*:
 - applicable to the management of bacterial BSIs;
 - used in clinical practice in the target setting at the time of the survey; *and/or*
- alternative representative drugs for each of the broader target antimicrobial groups considered in GLASS; *plus*
- any additional drugs routinely used or newly introduced in clinical practice in the target setting at the time of the survey and relevant to the clinical management of BSIs.

⁶ Includes patients investigated and treated for suspected BSI in the emergency department (emergency room/accident and emergency department) with delayed transfer to an inpatient ward.

⁷ *Escherichia coli*, *Klebsiella pneumoniae*, *Acinetobacter* spp., *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Salmonella* spp. (non-typhoidal), *Pseudomonas aeruginosa*, *Neisseria meningitidis*, *Haemophilus influenzae*, *Salmonella enterica* serovar Typhi, and *Salmonella enterica* serovar Paratyphi A.

6.3. Sample size calculation

Due to feasibility considerations, a survey should be powered at a minimum to estimate resistance with the desired precision for the most common organism in the target setting, which often corresponds to the SDG AMR indicator species (*E. coli*, *S. aureus*) or other GLASS target pathogens, for example, *K. pneumoniae*. This is achieved by taking the most conservative estimate for the expected resistance to an individual antibiotic (that is, that approaching 50%) and the most conservative

sample size that is operationally feasible (Box 4). Data for less common pathogens identified from blood cultures should be collected opportunistically until the sample for target bacterial species is reached. This approach will allow a description of the bacterial etiologies contributing to BSIs in the target setting and a description of the distribution of AMR across the contributing species, with resistance estimates to individual antimicrobials among less common bacterial pathogens being less precise than those for individual antimicrobials among the most frequent species.

Box 4. Sample size calculation

The sample size calculation should consider all data available for the previous calendar year in the target setting as follows:

- total number of plausible BSIs in the geographical setting to be studied;
- proportion of microbiologically confirmed BSIs (with positive culture);
- proportion of microbiologically confirmed BSIs due to the most frequent (target) bacterial species;
- expected prevalence of AMR, based on available data;
- desired precision of the estimate, to be expressed as a 95% confidence interval. The sampling uncertainty should be as low as possible, while ensuring that the corresponding calculated sample size is logistically feasible.

In the absence of data (that is, a-d above), an informed estimate must be made, based on the overall inpatient caseload in the previous calendar year (that is, number of inpatient admissions and/or inpatient days of care). For the expected prevalence of AMR (d), the most conservative estimate may be assumed (that is, 50%). The following formula should be used to calculate sample size under simple random sampling with a finite population correction:

$$n = \frac{N * z^2 * p * (1 - p)}{d^2 * (N - 1) + z^2 * p * (1 - p)}$$

where:

- N = total number of microbiologically confirmed BSI cases attributable to the most common clinically relevant bacterial species in the previous calendar year in the target setting;
- z = z-value (from the standard normal distribution) that corresponds to the desired confidence level (if confidence interval = 95%, $z = 1.96$);
- d = absolute precision (for instance, as a decimal, 7% should be expressed as 0.07);
- p = expected prevalence of AMR in the target bacterial species based on available data (for instance, as a decimal, 50% should be expressed as 0.5).

In the absence of previous survey data, a design effect of 2-3 should be assumed where cluster sampling is adopted, in which case the calculated sample size⁸ must be multiplied by 2 or 3. The sample size should also be increased to consider the patient pathway from case-finding activities and the expected potential losses. Briefly, if only 50% of microbiologically confirmed BSIs are due to the most common (target) bacterial species in the setting, and if only 10% of plausible BSIs are expected to yield a positive culture, the calculated sample for microbiologically confirmed BSIs due to the most common bacterial species, should be increased

by 50%, followed by 90%. Preliminary sample size simulations anticipate that in study designs involving cluster sampling (with design effect =2) and assuming 50% expected resistance to an individual antimicrobial in the most common bacterial species, approximately 7546 to 7834 individuals with suspected BSI should be enrolled in the survey to obtain approximately 755 to 783 microbiologically confirmed BSIs of which 50% are due to the target species. This sample would be needed to estimate the prevalence of resistance to an individual antimicrobial in the target species with 7% absolute precision in countries where the number

⁸ Obtained from the equation to calculate the sample size under simple random sampling, with a finite population correction.

of microbiologically confirmed BSIs due to the most common organism in the previous year (N) was between 5000 and 250 000. Thus, for the same absolute precision and expected prevalence of AMR, the sample size remains relatively stable for large values of N . The relative precision can be calculated as (absolute precision $[d]/$ expected prevalence of AMR $[p]) \times 100$ and should not be greater than 25% of p , where feasible, and never greater than 50% of p . In this example that assumes 7% absolute precision and 50% expected prevalence of AMR, the relative precision would be 14%.

6.4. Sampling strategy

During the planning stage of the survey, national authorities and technical personnel should assemble a sampling frame consisting of a complete, exhaustive list of acute care hospitals in the country from which to draw a sample (Box 5). The list should be compiled together with the number of plausible and/or microbiologically confirmed BSIs diagnosed in each facility during the previous calendar year (if available) and the inpatient caseload in the previous year. These data, along with the calculated sample size, will inform the most context-appropriate sampling strategy.

Box 5. Eligibility criteria for healthcare facilities

All hospitals in the country delivering acute inpatient care are eligible for participation in the survey and should be included in the sampling frame from which a sample of facilities is drawn. **Acute care** involves short-term treatment for a severe injury or episode of illness, an urgent medical condition, or during recovery from surgery. By contrast, **long-term care** is care delivered to patients who need assistance to function in their daily lives. Non-acute healthcare facilities delivering long-term care only are not eligible to participate in a survey and must be excluded from the sampling frame. These include nursing homes, rehabilitation or psychiatric centres.

Healthcare facilities delivering acute care are divided into four categories according to the level of care delivered (that is, primary, secondary, tertiary and specialized). Within these, hospitals are distinguished from other types of medical facilities by their ability to admit and care for inpatients. An inpatient is a person who is formally admitted to hospital for an overnight stay and discharged after one or more days.

Sampling strategies span from simple to complex designs, the choice of which depends on the setting. In general, the simplest possible design is preferred. More complex designs may require larger sample sizes, more complex statistical analyses and may be more prone to bias. However, it is also critical to consider setting-specific logistical aspects and the capacity for implementation when choosing a survey design. Below are examples of sampling designs.

- Exhaustive sampling of all hospitals in the country (for example, in very small countries with manageable numbers of facilities, this approach will not incur the sampling design effects that occur in clustered surveys).
- Single-stage cluster sampling of hospitals (for example, where all hospitals present similar characteristics in terms of case-mix and inpatient caseload).
- Single-stage cluster sampling of geographical units (for example, where comprehensive nationwide mapping of hospitals is unavailable, or in very large countries where all hospitals in selected units are then enrolled in the survey).
- Stratified single-stage cluster sampling of hospitals (for example, where significant caseload and case-mix variation occurs between hospitals).
- Stratified multi-stage cluster sampling (for example, where the study needs cannot be addressed with simpler designs. This involves progressive sampling of smaller units within selected groups. The design may comprise stratified sampling of healthcare facilities as primary sampling units based on inpatient caseload, followed by sampling of inpatient wards within facilities as secondary units in the strata comprising medium and large hospitals, respectively. Prior sampling of administrative units may also be considered in very large geographical settings).

Two cluster sampling approaches may be considered, depending on the characteristics of hospitals in the target setting: (1) probability proportional to size sampling with replacement and fixed cluster size; or (2) constant probability sampling without replacement and variable cluster size. In both cases, patients are enrolled consecutively within selected hospitals until a fixed cluster size is reached (see 1), or for a fixed time period that is identical in all selected facilities (see 2). Both approaches lead to a sample that is proportional to the inpatient BSI caseload in each hospital. Stratified designs may involve the application of different sampling approaches (for example, exhaustive sampling; cluster sampling and fixed cluster size; cluster sampling and variable cluster size) independently to each stratum. We anticipate that the number of hospitals in the final sample will range from ≥ 30 (to improve the precision of the estimators) to ≤ 60 (for logistic and resource considerations).

6.5. Case finding, patient enrolment and data collection

A survey should be designed to ensure that all adult (≥ 18 years of age), paediatric (≥ 29 days and ≤ 17 years of age) and neonatal (≤ 28 days of age) patients seeking acute inpatient care and meeting the case definition for plausible BSI in the selected hospitals are correctly identified, have a blood sample drawn according to best clinical practices and that all samples undergo microbial identification and AST. Case definitions for plausible BSI are adapted from age-specific criteria, that is, the quick Sequential Organ Failure Assessment score for adults (24-26) and the Liverpool quick Sequential Organ Failure Assessment score for paediatric patients (26, 27), as well as criteria specific to the neonatal group (26, 28). In addition, clinicians should be at liberty to order blood cultures any time a BSI is suspected, even where the case definition is not met. Wherever feasible, electronic data collection using a combination of portable tablets and desktop computers should be prioritized over the use of paper-based forms; survey data should be collated into a dedicated database following good data and record management practices (20).

Patients meeting the case definition for BSI and/or with an indication for blood culture according to clinicians' criteria other than the case definition (these groups should be clearly differentiated in the database to better inform the analysis plan) should be enrolled into the survey at the time of sampling. Case finding involves screening all inpatients by reviewing clinical notes and by checking the signs and symptoms that conform to the case definition of plausible BSI. Wards and departments participating in the survey will keep a "screening and enrolment log" to facilitate the traceability of survey records, allow monitoring and audit activities, and inform the need for corrective measures (for example, re-training). The log will also include daily utilization summaries (for example, number of inpatients on the ward). At the time of enrolment, a minimum set of clinical and demographic information will be collected from each patient by completing a case report form. At the core level, the case report will include sufficient information to classify the suspected origin of the plausible BSI beyond reasonable doubt (that is, either community or hospital) and sufficient information to rule out any bias of laboratory test results due to prior antimicrobial therapy. A system should be developed to verify the prompt feedback of laboratory test results to clinicians and to ensure that adequate timely treatment is available to all patients (see [Section 6.10](#)).

6.6. Specimen referral and laboratory methods

Inoculated blood culture bottles should be processed by the hospital laboratory or packaged according to international regulations adopted by the International Air Transportation Association and shipped to the nearest quality assured microbiology laboratory if no such service is provided on-site. A quality assured reference laboratory for the selected testing methods (for example, the national or regional reference laboratory) should be available and linked to all intermediate laboratories providing diagnostic services to hospitals. Microbial identification and AST should be performed according to international standards (29, 30), as well as the European Committee on Antimicrobial Susceptibility Testing (EUCAST) recommendations (31) or the Clinical and Laboratory Standards Institute (CLSI) (32) methodology and guidance, in agreement with the standard of choice in the target setting. The survey should ensure the long-term storage of all isolates to facilitate external quality assurance activities, re-testing if/where required, and potential further investigations, including whole genome sequencing investigations, where appropriate.

The reference laboratory should ensure the quality of culture and AST performed by peripheral units by establishing a regular "on-site" supervision programme for these units and by providing training in laboratory procedures and access to quality assurance systems. An external quality assessment programme with a partner supranational reference laboratory should be established to validate the results of susceptibility tests done by the reference laboratory and any other relevant laboratories. In cases where microbiology diagnostics are not available on-site, a specimen referral system should be implemented to ensure the transport of specimens at ambient temperature to the nearest quality assured laboratory within the time window recommended for optimal laboratory processing of samples (that is, ideally ≤ 12 hours and up to 24 hours at 25°C (33)). A staggered survey design where groups of hospitals begin patient enrolment sequentially can help simplify specimen transportation arrangements when resources are limited by reducing the number of facilities referring samples to the laboratory at any point in time. In addition, in geographically-distant hospitals lacking on-site microbiology diagnostics, only culture bottles showing bacterial growth may be transported to the relevant laboratory. The advantage of this approach is that transportation delays are less critical for positive blood cultures (that is, after a monitoring system signals bacterial growth), except for the case of *S. pneumoniae* (34). The survey may use alternatives to continuous monitoring blood culture systems for the simplified detection of positive blood cultures, such as the use of special venting units that attach to the bottles, which allow for the rapid qualitative detection of bacterial growth, thus minimizing the need for blind subculturing and error-prone monitoring, interpretation and detection of growth by technical staff.

6.7. Data analysis

Survey-weighted generalized linear models with inverse probability weighting and design-based standard errors should be used to estimate the prevalence of resistance (and corresponding 95% confidence intervals) to selected antimicrobials and antimicrobial groups in the clinically relevant bacterial species identified. Statistical methods such as multiple imputation may be applied to reduce the risk of bias due to missing data if/where appropriate. Sampling weights, following consideration of the final survey design, may also be applied at the analysis stage to account for potential bias due to the over- or under-enrolment of patients with microbiologically confirmed BSI. The complete data analysis approach, including commented R code, has been published previously (13).

6.8. Survey governance

A survey is a demanding and challenging undertaking that depends largely on national human resources. Adequate numbers of appropriately qualified and trained manpower should be made available during the entire survey period without affecting routine activities. Each country should decide on the best governance model. Based on national prevalence surveys in other diseases, it is suggested that parties contributing to the management of a national survey and its implementation may be organized into three levels as described in [Box 6](#).

6.9. Survey monitoring and management

Tools should be developed in advance of implementing a survey to help manage anticipated risks and challenges and to ensure conformity with agreed procedures and good practice. These include the following minimum (essential) documentation to be prepared before the start of a survey.

A survey quality plan. A general document outlining the quality management system and the quality assurance and control measures that will be in place to satisfy the quality requirements for the survey.

A survey monitoring plan. A document detailing the survey monitoring schedule and strategy, as well as the tools (such as checklists and report templates) that will be used to document the training and preparedness of sites to start the survey and those that will be used to monitor survey sites and report on the findings.

A risk management plan. A document detailing proactive actions to identify, assess, monitor, report and respond to risks, including risks to sample quality, data integrity and protection of survey patient rights, safety and well-being.

Templates for developing these plans, as well as checklists, logs and forms to support survey management, supervision and monitoring can be adapted from existing sources (18). The schedule for conducting monitoring visits to all participating

Box 6. Example of governance arrangements for a national AMR prevalence survey

Scientific advisory committee. A technical oversight committee that provides supervision for the overall technical conduct of the survey. Technical oversight is often provided by national and international topic experts, including from WHO and non-governmental organizations.

National survey coordination team. Responsible for the operational oversight and day-to-day management of the survey. The survey coordination team is led by a designated principal investigator and requires strong official backing from the government authority responsible for health services. The team should include national experts from each of the main operational areas, as well as relevant programme managers from the national ministry of health (or designated persons), head of the central reference laboratory (or designated persons), and an epidemiologist and/or statistician.

Survey field teams. An operational team composed of central and peripheral personnel tasked with implementing the survey at the field level, such as staff in participating hospitals and laboratories. The field team reports progress and challenges to the coordination team and ensures the scientific and ethical integrity of the survey.

hospitals should be developed as part of the monitoring plan and budgeted for before the start of the survey. At a minimum, all facilities participating in the survey should be visited by the coordination team at least once during the patient intake period. After the initial visits, a flexible risk-based monitoring approach should be used. For example, hospitals may be contacted regularly by telephone to remotely identify those requiring further supervision through additional monitoring visits and/or more frequent telephone calls. At regular intervals during the patient intake period, all survey data should be tabulated and reviewed. A survey epidemiologist should make regular reports to the survey coordination team based on these tables, which should include selected survey quality and progress indicators related to enrolment, completeness of data, transport and logistics, laboratory results, etc. If monitoring activities and/or data reviews identify significant problems, the survey coordination team should develop a detailed plan to address these issues. Halfway through the survey, the national survey coordination team should hold a mid-term review meeting to discuss the quality of data collection, laboratory procedures, quality control results, and preliminary survey results, including interpretation. Additionally, an external monitoring review should be conducted by experts who are not members of the survey coordination team close to the start date of the intake period, but ensuring that sufficient data have been collected to allow a meaningful review.

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6.10. Ethical considerations

The principles and standards outlined for the ethical implementation of surveillance systems in public health should be followed (22). Sensitive patient information should be kept confidential outside the clinical team. All documents and tools produced during the planning stage (for example, protocol, data collection tools, standard

operating procedures, etc.), should be reviewed and approved by a relevant ethics committee or institutional review board prior to the implementation of the survey. Informed consent or assent should be obtained from individuals or their legally authorized representative, unless this is deemed unfeasible and provided that the local (national) ethics committee agrees to waive the need for explicit individual informed consent, allowing instead patients to “opt-out” after being notified and informed about the survey, including understandable and culturally-sensitive education material about the benefits of the procedures for diagnosis and treatment. All patients with an indication for blood culture at selected hospitals should have blood samples taken and will be provided with timely and appropriate treatment and care, regardless of their participation in the survey. In the event of a limited capacity to properly treat patients identified with drug-resistant infection, provisions should be put in place ahead of the survey to ensure that all people with drug-resistant BSIs have access to appropriate treatment according to the most recent recommendations from the WHO essential medicines lists (35, 36) and AWaRe antibiotic categorization (37).

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6.11. Dissemination of survey findings and policy and practice implications

A survey should facilitate policy discussion, promote capacity-building, and inform strategic planning and appropriate interventions. To effectively translate the survey findings into concrete action, national authorities should organize a broader stakeholder consultation upon completion of a survey to disseminate and discuss key findings, secure political commitment, and advocate for action nationally, prior to the formal dissemination of survey results to the national and international community.

7. Survey budget and timelines

National authorities should consider the survey as an opportunity for strengthening clinical, laboratory, logistic and data management capacity within the country. The required budget must be carefully calculated and all necessary funds must be available before the start of the survey. The budget will depend on the following elements: the number of participant hospitals; the required sample; coverage of diagnostic tests and treatment by insurance schemes or other existing funding streams; need to institute a rapid referral system or deploy equipment (if applicable); training and monitoring activities; recruitment; and

procurement. As an example, the current average cost of a national prevalence survey to estimate the prevalence of drug resistance in tuberculosis typically does not exceed US\$ 400 000 (13).

An example of timelines for individual survey activities are summarized in Table 3. Survey planning, implementation and dissemination activities are expected to be completed within 18-24 months, depending on the survey organization and the required patient intake period, which is in turn determined by the study design and the sample size.

Table 3. Example of activities and timeframes for the development of survey timelines⁹

Survey planning	8 months
Formation of survey team and advisory committee	1 month
Development of survey protocol and other essential documents (standard operating procedures, etc.)	3 months
Database development and testing	3 months
Ethics approval	1 month
Staff recruitment	3 months
Procurement and distribution of supplies	3 months
Training of field staff	2 months
Pilot of survey procedures	1 month
Launch of full survey (patient enrolment, laboratory activities, monitoring, etc.)	12 months
External quality assurance of laboratory test results	12 months
Analysis, interpretation and dissemination of survey findings	4 months
Data analysis and report writing	3 months
National stakeholder workshop/s	1 month

⁹ The listed activities and respective timelines are based on experiences from national prevalence surveys of drug-resistant tuberculosis.

References

1. Ten threats to global health in 2019. Geneva: World Health Organization; 2019 (<https://www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019>, accessed 31 December 2022).
2. Murray CJ, Ikuta KS, Sharara F, Swetschinski L, Robles Aguilar G, Gray A, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet*. 2022; 399: 629-55. doi: 10.1016/s0140-6736(21)02724-0.
3. Laxminarayan R, Sridhar D, Blaser M, Wang M, Woolhouse M. Achieving global targets for antimicrobial resistance. *Science*. 2016;353:874-5. doi: 10.1126/science.aaf9286.
4. Klein EY, Van Boeckel TP, Martinez EM, Pant S, Gandra S, Levin SA, et al. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proc Natl Acad Sci*. 2018;115:E3463-E70. doi:10.1073/pnas.1717295115.
5. Global action plan on antimicrobial resistance. Geneva: World Health Organization; 2015 (<http://www.who.int/antimicrobial-resistance/global-action-plan/en/>, accessed 31 December 2022).
6. Global antimicrobial resistance and use surveillance system (GLASS). Geneva: World Health Organization; 2015 (<https://www.who.int/initiatives/glass>, accessed 31 December 2022).
7. Global antimicrobial resistance surveillance system: manual for early implementation. Geneva: World Health Organization; 2015 (<https://apps.who.int/iris/handle/10665/188783>, accessed 31 December 2022).
8. Global antimicrobial resistance and use surveillance system (GLASS) report: 2021. Geneva: World Health Organization; 2021 (<https://www.who.int/publications/i/item/9789240027336>, accessed 31 December 2022).
9. Global indicator framework for the Sustainable Development Goals and targets of the 2030 Agenda for Sustainable Development. New York, NY: United Nations Statistics Division; 2017 (<https://unstats.un.org/sdgs/indicators/indicators-list/>, accessed 31 December 2022).
10. IAEG-SDGs 2020 Comprehensive Review Proposals Submitted to the 51st session of the United Nations Statistical Commission for its consideration. New York, NY: United Nations Statistics Division 2020 (<https://unstats.un.org/sdgs/iaeg-sdgs/2020-comprev/UNSC-proposal/>, accessed 31 December 2022).
11. Methods for surveillance of antimalarial drug efficacy. Geneva: World Health Organization; 2009 (<https://www.who.int/publications/i/item/9789241597531>, accessed 31 December 2022).
12. Report on antimalarial drug efficacy, resistance and response: 10 years of surveillance (2010-2019). Geneva: World Health Organization; 2020 (<https://www.who.int/publications/i/item/9789240012813>, accessed 31 December 2022).
13. Guidance for the surveillance of drug resistance in tuberculosis, sixth edition. Geneva: World Health Organization; 2021 (<https://www.who.int/publications/i/item/9789240018020>, accessed 31 December 2022).
14. Global tuberculosis report 2020. Geneva: World Health Organization; 2020 (<https://www.who.int/publications/i/item/9789240013131>, accessed 31 December 2022).
15. HIV drug resistance surveillance. Geneva: World Health Organization; 2022 (<https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hiv/treatment/hiv-drug-resistance/hiv-drug-resistance-surveillance>, accessed 31 December 2022).
16. HIV drug resistance report 2021. Geneva: World Health Organization; 2021 (<https://www.who.int/publications/i/item/9789240038608>, accessed 31 December 2022).
17. Cassini A, Högberg LD, Plachouras D, Quattrocchi A, Hoxha A, Simonsen GS, et al. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. *Lancet Infect Dis*. 2019;19:56-66. doi: 10.1016/s1473-3099(18)30605-4.

18. Good practices guidance handbook for national TB surveys: how to apply good clinical and good data management practices for national TB surveys. Geneva: World Health Organization; 2022 (<https://www.who.int/publications/i/item/9789240028654>, accessed 31 December 2022).
19. Step 4 in Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6 (R2). Geneva: International Council for Harmonisation (ICH); 2016 (https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf, accessed 31 December 2022).
20. Technical report series 996-Annex 5: WHO good data and record management practices. WHO expert committee on specifications for pharmaceutical products. Geneva: World Health Organization; 2016 (<https://www.who.int/publications/m/item/trs-966---annex-5-who-good-data-and-record-management-practices>, accessed 31 December 2022).
21. Tuberculosis prevalence surveys: a handbook. Geneva: World Health Organisation; 2011 (<https://www.who.int/publications/i/item/9789241548168>, accessed 31 December 2022).
22. WHO guidelines on ethical issues in public health surveillance. Geneva: World Health Organization; 2017 (<https://apps.who.int/iris/bitstream/handle/10665/255721/9789241512657-eng.pdf>, accessed 31 December 2022).
23. Global antimicrobial resistance and use surveillance system: GLASS-AMR manual, second edition. Geneva: World Health Organization; 2023 (in press).
24. Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, et al. Assessment of clinical criteria for sepsis: for the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315:762-74. doi: 10.1001/jama.2016.0288.
25. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315:801-10. doi: 10.1001/jama.2016.0287.
26. Turner P, Ashley EA, Celhay OJ, Douangnouvong A, Hamers RL, Ling CL, et al. ACORN (A Clinically-Oriented Antimicrobial Resistance Surveillance Network): a pilot protocol for case based antimicrobial resistance surveillance. *Wellcome Open Res*. 2020;5:13. doi: 10.12688/wellcomeopenres.15681.2.
27. Romaine ST, Potter J, Khanijau A, McGalliard RJ, Wright JL, Sefton G, et al. Accuracy of a modified qSOFA Score for predicting critical care admission in febrile children. *Pediatrics*. 2020;146. doi: 10.1542/peds.2020-0782.
28. Vergnano S, Buttery J, Cailles B, Chandrasekaran R, Chiappini E, Clark E, et al. Neonatal infections: case definition and guidelines for data collection, analysis, and presentation of immunisation safety data. *Vaccine*. 2016;34:6038-46. doi: 10.1016/j.vaccine.2016.03.046.
29. Standards for microbiology investigations (UK SMI). UK Health Security Agency; 2022 (<https://www.gov.uk/government/collections/standards-for-microbiology-investigations-smi>, accessed 31 December 2022).
30. Seale AC, Gordon NC, Islam J, Peacock SJ, Scott JAG. AMR surveillance in low and middle-income settings - A roadmap for participation in the Global Antimicrobial Surveillance System (GLASS). *Wellcome Open Res*. 2017;2:92. doi: 10.12688/wellcomeopenres.12527.1.
31. The European Committee on Antimicrobial Susceptibility Testing (EUCAST). 2022 (<https://www.eucast.org/>, accessed 31 December 2022).
32. Clinical and Laboratory Standards Institute (CLSI). 2022 (<https://clsi.org/>, accessed 31 December 2022).
33. Ling CL, Roberts T, Soeng S, Cusack T-P, Dance DAB, Lee SJ, et al. Impact of delays to incubation and storage temperature on blood culture results: a multi-centre study. *BMC Infect Dis*. 2021 21:1. 2021;21:1-8. doi: 10.1186/S12879-021-05872-8.
34. Roberts T, Chandna A, Watthanaworawit W, Thaiprakong A, Soeng S, Simmalavong M, et al. Impact of delayed processing of positive blood cultures on organism detection: a prospective multi-centre study. *BMC Infect Dis*. 2022;22. doi: 10.1186/s12879-022-07504-1.
35. WHO Model List of Essential Medicines, 22nd List. Geneva: World Health Organization; 2021 (<https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2021.02>, accessed 31 December 2022).
36. WHO Model List of Essential Medicines for Children, 8th List. Geneva: World Health Organization; 2021 (<https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2021.03>, accessed 31 December 2022).
37. The 2019 WHO AWaRe classification of antibiotics for evaluation and monitoring of use. Geneva: World Health Organization; 2019 (<https://apps.who.int/iris/handle/10665/327957>, accessed 31 December 2022).

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