Indicator Proposal Summary

Full name of the Indicator: Reduce the percentage of bloodstream infections due to selected antimicrobial resistant organisms

(Possible indicator number: 3.d.2 to measure progress against target SDG 3.d)

Custodian Agencies: World Health Organization

Goals and targets addressed:

Goal 1: End poverty in all its forms everywhere

TARGET 1.1: By 2030, eradicate extreme poverty for all people everywhere, currently measured as people living on less than $1.25 a day

Goal 2: End hunger, achieve food security and improved nutrition and promote sustainable agriculture

TARGET 2.1: By 2030, end hunger and ensure access by all people, in particular the poor and people in vulnerable situations, including infants, to safe, nutritious and sufficient food all year round

Goal 3: Ensure healthy lives and promote well-being for all at all ages

TARGET 3.1: By 2030, reduce the global maternal mortality ratio to less than 70 per 100,000 live births

TARGET 3.2: By 2030, end preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under-5 mortality to at least as low as 25 per 1,000 live births

TARGET 3.3: By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases

TARGET 3.8: Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all.

TARGET 3.9: By 2030, substantially reduce the number of deaths and illnesses from hazardous chemicals and air, water and soil pollution and contamination.

TARGET 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

GOAL 6: Ensure availability and sustainable management of water and sanitation for all

TARGET 6.1: By 2030, achieve universal and equitable access to safe and affordable drinking water for all

TARGET 6.2: By 2030, achieve access to adequate and equitable sanitation and hygiene for all and end open defecation, paying special attention to the needs of women and girls and those in vulnerable situations

TARGET 6.3: By 2030, improve water quality by reducing pollution, eliminating dumping and minimizing release of hazardous chemicals and materials, halving the proportion of untreated wastewater and substantially increasing recycling and safe reuse globally

GOAL 12: Ensure sustainable consumption and production patterns

TARGET 12.4: By 2020, achieve the environmentally sound management of chemicals and all wastes throughout their life cycle, in accordance with agreed international frameworks, and significantly reduce their release to air, water and soil in order to minimize their adverse impacts on human health and the environment.

What type of proposal (replacement, refinement, adjustment and addition), for replacement, refinement and adjustment, please list the original indicator and its number: Addition

1. Background and rationale for the indicator proposal

Antimicrobial resistance (AMR) is a global threat to health, livelihoods and the achievement of many of the Sustainable Development Goals noted in the earlier section. Antibiotics, antivirals, antiparasitic agents and antifungals are increasingly ineffective owing to resistance developed through their excessive or inappropriate use, with serious consequences for human and animal health (terrestrial and aquatic), and plant health, and negative impacts on food production, the environment and the global economy.

Antimicrobial resistance will negatively impact the achievement targets (3.1, 3.2, 3.3, 3.8, 3.9, 3.d) listed earlier under Goal 3 due to reduced treatment options for infections by resistant pathogens, will impact target (2.1) under Goal 2 by impacting the agricultural productivity, including food animal production, and will impact target (1.1) in Goal 1 as increased antimicrobial resistance will result in large declines in economic growth, increase economic inequality and drive an additional 24 million people into extreme poverty by 2030[1].

Achieving many of the targets under Goal 3 (3.8, 3.d), Goal 6 (6.1, 6.2, 6.3) , and Goal 12 (12.4) would also positively impact the burden of antimicrobial resistance in countries and help address the crisis.

The SDGs, when they were being developed, did not consider the need for a specific indicator on addressing antimicrobial resistance as a national and global risk. However, there has been significant increase in global political attention to this issue, to its cross-cutting nature, and devastating impact for populations in low- and middle-income countries. Since 2015, a global action plan on AMR has been developed and endorsed by the governing bodies of WHO, FAO and OIE (World Organisation for Animal Health) through specific resolutions calling for increased attention and action on combatting antimicrobial resistance. In addition, in 2016, member states of the United Nations adopted a "political declaration at the high-level meeting of the UN General Assembly on antimicrobial resistance," called for a "One Health " approach to addressing AMR. Most recently, in 2019, the Inter-agency Coordination Group on AMR that was established by the UN Secretary-General, delivered its key recommendations that called for urgent action in countries and global monitoring. The UN Secretary-General has also recently (in May 2019) submitted a comprehensive report on AMR to the UN General Assembly that calls for scaled up technical assistance to countries.

Given the above context, and the urgent need to build country capacity to address this growing national and global multisectoral risk, it is critical that the proposed additional indicator on AMR be considered for inclusion in the list of SDG Indicators. This new indicator, while providing data to monitor the trend globally, will also be very effective as a proxy for tracking progress of enhancing country capacity to effectively implement their national action plans on AMR. It will also ensure political attention to addressing AMR at the country-level, through the national SDG Committees.

Information on how and when the methodology has become an international standard and who is the governing body that approves it

AMR surveillance is the cornerstone for assessing the burden of AMR and for providing the necessary information for action in support of local, national and global strategies.

Global surveillance programmes that monitor resistance in specific bacterial pathogens, such as Mycobacterium tuberculosis and Neisseria gonorrhoeae, have been in place for many years. In addition, a number of regional surveillance programmes have been monitoring resistance in selected geographical areas, such as the Central Asian and Eastern European Surveillance of Antimicrobial

[1] World Bank Group, *Drug-resistant Infections: A Threat to Our Economic Future – Final Report* (Washington, D.C., March 2017).

Resistance (CAESAR), the European Antimicrobial Resistance Surveillance Network (EARS-Net) and the Latin American Antimicrobial Resistance Surveillance Network (ReLAVRA). Despite the success of these programmes in gathering data over many years, significant gaps remain in surveillance of many other bacterial pathogens that cause common infections in humans. To address these gaps, and build common standards for methods, data-sharing and coordination at local, national, regional and global levels, WHO introduced an agreed surveillance approach in December 2014.

The global antimicrobial resistance surveillance systems (GLASS) of WHO enables standardized, comparable and validated data on AMR to be collected, analysed and shared with countries, in order to inform decision-making, drive local, national and regional action and provide the evidence base for action and advocacy.

The methodology for the proposed indicator is a sub-set of a more comprehensive methodology developed by GLASS. The GLASS approach has been well recognised by Member States and leading scientific bodies. The methodology for the proposed indicator is also similar to that used by the European Antimicrobial Resistance Surveillance Network (EARS-Net) to collect harmonised AMR data across EU member states and other European countries.[2]

GLASS will collect, analyse and report harmonized data on infected patients, aggregated at national level. The objectives of GLASS are to: 1) foster national surveillance systems and harmonized global standards; 2) estimate the extent and burden of AMR globally by selected indicators; 3) analyse and report global data on AMR on a regular basis; 4) detect emerging resistance and its international spread; 5) inform implementation of targeted prevention and control programmes; and 6) assess the impact of interventions. Use of the surveillance standards proposed in GLASS could also improve patient safety by promoting diagnostic stewardship for responsible use of antimicrobial agents and ensuring quality-assured, standardized identification of bacteria and antimicrobial susceptibility testing (AST) in patient management.

Early implementation of GLASS will cover the period 2015–2019 and includes an implementation manual for countries[3]. During this period, GLASS will provide the standards and tools for routine surveillance based on microbiological and clinical information on priority bacterial infections in humans, start country enrolment and produce global reports on GLASS implementation and AMR rates.

GLASS will initially concentrate on the antibiotic-resistant bacteria that are the greatest threats globally (see Table 1.), particularly those that are resistant to several drugs thereby limiting therapeutic options.

For the proposed indicator, frequency of bloodstream infection among hospital patients' due to two selected resistant pathogens - methicillin-resistant Staphylococcus aureus (MRSA) and Escherichia coli resistant to 3rd-generation cephalosporin (e.g., ESBL- E. coli) – will be used.

[2] https://ecdc.europa.eu/sites/portal/files/documents/EARS-Net%20reporting%20protocol%202018.%20docx.pdf

[3] https://apps.who.int/iris/bitstream/handle/10665/188783/9789241549400_eng.pdf?sequence=1

Table 1. Pathogen-antimicrobial combinations on which GLASS will gather data

Pathogen	Antibacterial class	Antibacterial agents that may be used for AST[a,b]
Escherichia coli	Sulfonamides and trimethoprim	Co-trimoxazole
	Fluoroquinolones	Ciprofloxacin or levofloxacin
	Third-generation cephalosporins	Ceftriaxone or cefotaxime and ceftazidime
	Fourth-generation cephalosporins	Cefepime
	Carbapenems[c]	Imipenem, meropenem, ertapenem or doripenem
	Polymyxins	Colistin
	Penicillins	Ampicillin
Klebsiella pneumoniae	Sulfonamides and trimethoprim	Co-trimoxazole
	Fluoroquinolones	Ciprofloxacin or levofloxacin
	Third-generation cephalosporins	Ceftriaxone or cefotaxime and ceftazidime
	Fourth-generation cephalosporins	Cefepime
	Carbapenems[c]	Imipenem, meropenem, ertapenem or doripenem
	Polymyxins	Colistin
Acinetobacter baumannii	Tetracyclines	Tigecycline or minocycline
	Aminoglycosides	Gentamicin and amikacin
	Carbapenems[c]	Imipenem, meropenem or doripenem
	Polymyxins	Colistin
Staphylococcus aureus	Penicillinase-stable beta-lactams	Cefoxitin[d]
Streptococcus pneumoniae	Penicillins	Oxacillin[e]
		Penicillin G
	Sulfonamides and trimethoprim	Co-trimoxazole
	Third-generation cephalosporins	Ceftriaxone or cefotaxime
Salmonella spp.	Fluoroquinolones	Ciprofloxacin or levofloxacin
	Third-generation cephalosporins	Ceftriaxone or cefotaxime and ceftazidime
	Carbapenems[c]	Imipenem, meropenem, ertapenem or doripenem
Shigella spp.	Fluoroquinolones	Ciprofloxacin or levofloxacin
	Third-generation cephalosporins	Ceftriaxone or cefotaxime and ceftazidime
	Macrolides	Azithromycin
Neisseria gonorrhoeae	Third-generation cephalosporins	Cefixime
		Ceftriaxone
	Macrolides	Azithromycin
	Aminocyclitols	Spectinomycin
	Fluoroquinolones	Ciprofloxacin
	Aminoglycosides	Gentamicin

a The listed substances are priorities for 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.

b One of more of the drugs listed may be tested in countries. S, I, R and nominator and denominator data for each shall be reported separately.

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

d Cefoxitin is a surrogate for testing susceptibility to oxacillin (methicillin, nafcillin); the AST report to clinicians should state susceptibility or resistance to oxacillin.

e Oxacillin is a surrogate for testing reduced susceptibility or resistance to penicillin: the AST report to clinicians should state reduced susceptibility or resistance to penicillin.

Data sources and data availability

GLASS combines patient, laboratory and epidemiological surveillance data to enhance understanding of the extent and impact of AMR on populations. Cases will be detected from the results of antimicrobial susceptibility testing (AST) of specimens sent to laboratories and core clinical information.

Cases will be found among routine clinical samples by AST of defined specimen types from patients selected for sampling at surveillance sites according to local practice. Basic demographic and epidemiological information will be collected on each patient and on the population covered to identify their characteristics. AST results will thus be combined with the patient data that accompany every request for AST and related to population data from the surveillance site.

Data on bacterial resistance in human infections to be entered into GLASS will be obtained from the following specimens: blood, urine, faeces, urethral and cervical swabs (Table 2).

Table 2. Priority specimens and pathogens for surveillance of AMR

Specimen	Laboratory case definition	Surveillance type and sampling setting	Priority pathogens for surveillance
Blood	Isolation of pathogen from blood[a]	Selected sites or national coverage Continuous Patients in hospital and in the community	*E. coli* *K. pneumoniae* *A. baumannii* *S. aureus* *S. pneumoniae* *Salmonella* spp.
Urine	Significant growth in urine specimen[b]	Selected sites or national coverage Continuous Patients in hospital and in the community	*E. coli* *K. pneumoniae*
Faeces	Isolation of *Salmonella* spp.[c] or *Shigella* spp. from stools	Selected sites or national coverage Continuous Patients in hospital and in the community	*Salmonella* spp. *Shigella* spp.
Urethral and cervical swabs	Isolation of *N. gonorrhoeae*	Selected sites or national coverage Continuous Patients in hospital and in the community	*N. gonorrhoeae*

[a] Any pathogen isolated from a blood culture may be significant for surveillance locally and nationally; only the prioritized pathogens for global surveillance are listed here.

[b] Pure culture according to local laboratory practice. Catheter samples should be excluded if possible.

[c] Diarrhoeal surveillance is for non-typhoid salmonella species; for local clinical purposes, typhoid and paratyphoid should be included.

The surveillance targets for GLASS are: all patients sampled for prioritized specimens (both positive and negative samples); all patients sampled for prioritized specimens with growth of priority species (only positive samples).

Surveillance should be continuous and aggregated at national level every 12 months and as per the national surveillance schedule.

During early implementation of GLASS, AST results will be classified according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI) or the European Committee on Antimicrobial Susceptibility Testing (EUCAST). The results for the priority pathogens and antibiotics will be classified as susceptible (S), intermediate (I), resistant (R), or not tested or not applicable.

For the purposes of early implementation of GLASS, countries will be requested to submit the following information:

- the total national population;
- the numbers of patients seeking care over 12 months at surveillance sites in outpatient clinics (e.g. number of consultations) and in inpatient facilities; and
- the numbers of patients with positive and negative cultures per specimen type and with susceptible and non-susceptible pathogens for each priority pathogen–antibiotic combination per specimen type, stratified according to core patient data:
    - age: the age groups reported in the Global Health Observatory;
    - gender;
    - hospital or other type of in-patient care facility: patient admitted for > 2 calendar days when the specimen was taken or admitted to the health care facility for < 2 calendar days but transferred from another health care facility where he or she was admitted for ≥ 2 calendar days; and
    - community: patients cared for at outpatient clinics or patients in hospital for ≤ 2 calendar days when the specimen was taken.

Specimens collected from hospital patients will be used as a proxy for hospital-acquired infections, and those collected from patients in the community will be considered a proxy for community infections.

All data must be aggregated at national level before submission to GLASS. It is recommended that the surveillance coordination centre maintain individual data for detection of errors and quality control. The WHONET software has been adapted to facilitate data entry at surveillance sites, reporting to national surveillance centres and aggregation of data at national level for automatic generation of the reporting forms.

Table 3: Number of countries currently enrolled and providing AMR data to GLASS

Database	Number of countries enrolled	Number of countries reporting AMR data	Source
GLASS	78	47*	Ministries of Health

Footnote: The data are compiled by GLASS, World Health Organization. * - the number will be updated after 31 July, 2019 after the end of the current Datacol.

2. Confirmation/explanation of joint submission with other partner/co-custodian agencies (if applicable)

Not Applicable

3. Conclusion

The proposed indicator captures crucial information on a growing national and global risk that impacts multiple sectors – human health, animal health, plant health, food production, environment, and directly impact poverty and economic development.

The current SDG indicator framework does not capture trends in AMR, or country capacity to address this risk. The growing political attention to the global risk of AMR necessitates the inclusion of an AMR indicator in the SDGs, and thereby, help ensure consistent monitoring and reporting at the country-level and global level.

The methodology for the proposed indicator has been tested and used by WHO for 5 years, and by the European Centre for Disease Prevention and Control and its European Antimicrobial Resistance Surveillance Network (EARS-Net) since 1998.

The GLASS methodology has the support of all 194 Member States of WHO, and was developed in consultation with experts from 30 countries in 2014.