Progress of implementation of WHO GLASS recommendations on priority pathogen-antibiotic sensitivity testing in Africa: A protocol for a scoping review

Mackline Hope, Dathan M Byonanebye, Jonathan Mayito, Reuben Kiggundu, Dickson Tabajjwa, Andrew Kambugu, Francis Kakooza

Submitted to: JMIR Research Protocols
on: March 07, 2024

Table of Contents

Progress of implementation of WHO GLASS recommendations on priority pathogen-antibiotic sensitivity testing in Africa: A protocol for a scoping review

Mackline Hope[1*] MBChB, MPH, DTMH; Dathan M Byonanebye[1*] MBChB, MMed, MPH, PhD; Jonathan Mayito[1*] MBChB, MMed, PhD; Reuben Kiggundu[1*] MBChB, MScPhysiology, MPH; Dickson Tabajjwa[1*]; Andrew Kambugu[1*] MBChB, MMed; Francis Kakooza[1*] PhD

[1]Infectious Diseases Institute Kampala UG
[*]these authors contributed equally

Corresponding Author:
Mackline Hope MBChB, MPH, DTMH
Infectious Diseases Institute
MKC Building, Makerere University, P.O Box 22418
Kampala
UG

Abstract

Background: Antimicrobial resistance (AMR) is a major global public health concern, particularly in low- and middle-income countries (LMICs) where resources and infrastructure for an adequate response are limited. The World Health Organization (WHO) Global Antimicrobial Resistance Surveillance System (GLASS) was introduced in 2016 to address these challenges, outlining recommendations for priority pathogen-antibiotic combinations. Despite this initiative, implementation in Africa remains understudied. This scoping review aims to assess the current state of implementing WHO GLASS recommendations on antimicrobial sensitivity testing (AST) in Africa.

Objective: The primary objective of this study is to determine the current state of implementing the WHO GLASS recommendations on AST for priority pathogen-antimicrobial combinations. The review will further document if reporting of AST results is according to: “susceptible”, “intermediate” and “resistant” recommendations according to GLASS.

Methods: Following Arksey and O'Malley's methodological framework, studies published between January 2016 and November 2023 will be included. Search strategies will target electronic databases, grey literature, and reference lists. Eligible studies will document isolates tested for antimicrobial sensitivity, focusing on WHO priority specimens and pathogens. Data extraction will focus on key study characteristics, study context, population, and adherence to WHO GLASS recommendations on AST

Results: Results are expected in August 2024, providing insights into the progress of GLASS implementation in Africa. Findings will inform current and future practices of AMR surveillance, identify gaps in implementation, and suggest strategies for improvement.

Conclusions: To our knowledge, this scoping review will be the first to comprehensively examine the implementation of WHO GLASS recommendations in Africa, shedding light on the challenges and successes of AMR surveillance in the region. By addressing these issues, it aims to contribute to global efforts to combat antimicrobial resistance.

(JMIR Preprints 07/03/2024:58140)
DOI: https://doi.org/10.2196/preprints.58140

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

✓ **Please make my preprint PDF available to anyone at any time (recommended).**
Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.
Only make the preprint title and abstract visible.
No, I do not wish to publish my submitted manuscript as a preprint.

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✔ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**

Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain v

Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <a href="http

Original Manuscript

Progress of implementation of WHO GLASS recommendations on priority pathogen-antibiotic sensitivity testing in Africa: A protocol for a scoping review.

Mackline Hope[1], Dickson Tabajjwa[1], Dathan M Byonanebye[1], Jonathan Mayito[1], Reuben Kiggundu[1], Andrew Kambugu[1], Francis Kakooza[1]

Abstract.

Background

Antimicrobial resistance (AMR) is a major global public health concern, particularly in low- and middle-income countries (LMICs) where resources and infrastructure for an adequate response are limited. The World Health Organization (WHO) Global Antimicrobial Resistance Surveillance System (GLASS) was introduced in 2016 to address these challenges, outlining recommendations for priority pathogen-antibiotic combinations. Despite this initiative, implementation in Africa remains understudied. This scoping review aims to assess the current state of implementing WHO GLASS recommendations on antimicrobial sensitivity testing (AST) in Africa.

Objectives.

The primary objective of this study is to determine the current state of implementing the WHO GLASS recommendations on AST for priority pathogen-antimicrobial combinations. The review will further document if reporting of AST results is according to: “susceptible”, “intermediate” and “resistant” recommendations according to GLASS.

Methods

Following Arksey and O'Malley's methodological framework, studies published between January 2016 and November 2023 will be included. Search strategies will target electronic databases, grey literature, and reference lists. Eligible studies will document isolates tested for antimicrobial sensitivity, focusing on WHO priority specimens and pathogens. Data extraction will focus on key study characteristics, study context, population, and adherence to WHO GLASS recommendations on AST.

Results

Results are expected in August 2024, providing insights into the progress of GLASS implementation in Africa. Findings will inform current and future practices of AMR surveillance, identify gaps in implementation, and suggest strategies for improvement.

Conclusions:

To our knowledge, this scoping review will be the first to comprehensively examine the implementation of WHO GLASS recommendations in Africa, shedding light on the challenges and successes of AMR surveillance in the region. By addressing these issues, it aims to contribute to global efforts to combat antimicrobial resistance.

Trial Registration: None

Keywords: Antimicrobial resistance; AMR; GLASS implementation; Surveillance; Africa

Introduction.

Drug resistant infections are a leading cause of morbidity and mortality, with 1.5 million related deaths reported in 2019(1). Low- and middle-income countries disproportionately face challenges associated with communicable diseases, yet there is limited data on the epidemiology and impact of antimicrobial resistance (AMR) in these regions(2). Currently there is limited data available on the geographical distribution of resistance, and conducting comprehensive population-based surveillance poses considerable challenges(3-6). The 2014 World Health Organization report on global surveillance of antimicrobial resistance (AMR) emphasized the lack of information regarding pathogens that pose significant public health risks(7). Assessing and monitoring AMR trends globally is limited by lack of quality data(8).

AMR surveillance systems are fundamental elements of infectious disease management(6) and provide the basis for a deeper comprehension of antimicrobial resistance spread(9). AMR surveillance data can enhance public health, guide health policy decisions, prompt responses to health crises, offer early alerts about emerging threats, and identify longstanding resistance patterns(6). In low- and middle-income countries, the capability for surveillance of antimicrobial resistance (AMR) varies(9), with Sub-Saharan Africa and Southeast Asia exhibiting the least developed coverage compared to high-income countries(10-12). In low-income areas like Africa, AMR surveillance challenges are significant due to weak infrastructure, limited resources, lack of trained staff, and various socioeconomic factors(13, 14). Despite the above challenges faced , a number of countries in Africa are implementing the WHO GLASS recommendations on AMR surveillance (15). This is in addition to other tools like the Global Action Plan (GAP) and the WHO benchmarks(16).

Antimicrobial resistance (AMR) surveillance is one of the five strategic objectives of the AMR GAP(3). To inform surveillance, the WHO launched the Global AMR Surveillance System (GLASS) manual in 2015(15) to standardize surveillance, including AST. The WHO GLASS manual makes

several recommendations on AMR surveillance systems. Among these include recommendations on priority specimens and pathogens for AMR surveillance of routine clinical samples(15). Additionally, the WHO has identified priority antibiotics for which monitoring of resistance should be done, **table 1**(15). To achieve this, the GLASS manual recommends pathogen–antimicrobial combinations on which GLASS gathers data(15).

The antimicrobial substances against which resistance or non-susceptibility will be monitored were selected because either they are commonly recommended first-line treatment or surrogate substances for resistance in drugs commonly used to treat patients, or the pathogen–antimicrobial combination is of particular concern because of limited treatment options. The recommended priority specimens include blood, urine, faeces, urethral and cervical swabs, **table 2**(15). The priority specimens were selected because they can be used to isolate pathogens that cause most of the common human infections in the blood stream, urinary tract, gastrointestinal tract, and genital/reproductive tract. The purpose of using priority specimens and pathogens was to enable systematic capacity building for countries as they set up their national AMR surveillance programs(17). Despite these recommendations, countries could also report on additional specimens and pathogens if national capacity for surveillance of these organisms exists.

Although GLASS manual was rolled out in 2016, the extent of its implementation specifically for priority specimen and pathogen-antibiotic combinations has not been fully explored especially in Africa. We aim to review existing literature to fill this knowledge gap and inform current and future practices of AMR surveillance. Specifically, we shall review, summarize, and report on priority specimen, pathogen-antibiotic combinations testing and reporting in the context of the WHO GLASS manual.

Table 1: Pathogen-antimicrobial combinations on which GLASS gathers data.

Pathogen	Antibacterial class	Antibacterial agents that may be used for AST[a,b]
Escherichia Coli	Sulphonamides and trimethoprim	Co-trimoxazole
	Fluoroquinolones	Ciprofloxacin or levofloxacin
	Third generation cephalosporins	Ceftriaxone or cefotaxime and ceftazidime
	Fourth generation cephalosporins	Cefepime
	Carbapenems	Imipenem, meropenem, ertapenem or doripenem
	Polymyxins	Colistin
	Penicillins	Ampicillin
Klebsiella pneumoniae	Sulphonamides and trimethoprim	Co-trimoxazole
	Fluoroquinolones	Ciprofloxacin or levofloxacin
	Third generation cephalosporins	Ceftriaxone or cefotaxime and ceftazidime

	Fourth generation cephalosporins	Cefepime
	Carbapenems	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
	Sulphonamides 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 or 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.

Table 2: Priority specimens and pathogens

Priority specimens	Priority pathogens
Blood stream infections	K. pneumoniae
	A. baumannii
	S. aureus
	S. pneumoniae

	Salmonella spp.
Urinary tract infections	E. coli K. pneumoniae
Acute diarrhoea	Salmonella spp. Shigella spp.

Methods

Study eligibility

The primary objective of this study is to determine the current state of implementing the WHO GLASS recommendations on AST for priority pathogen-antimicrobial combinations. We shall use a scoping review to map concepts around the study topic. The methodological framework proposed by Arksey and O'Malley 6-step scoping review process will be adopted for this proposed review(18). The PRISMA guidance for scooping reviews will be used for reporting the study findings(19). The inclusion criteria will be based on the population, concept, and context framework as proposed by the JBI for scoping reviews as a less restricted alternative to the population, intervention, comparator, outcome (PICO) framework(20). We anticipate that the methodologies of the studies will be more diverse, including observational studies, Randomized Controlled trials (RCTs), cohort and mixed methods studies. We will include only published and peer reviewed articles.

Inclusion criteria:

Original research articles and short reports with primary data.

Exclusion criteria:

1. Editorials, commentaries, review papers or any other publication without primary data.
2. Studies with insufficient data regarding the study question
3. Studies not published in English
4. Studies published before 2016

Study population

The scoping review will include studies that document isolates collected and tested for antimicrobial

sensitivity in Africa. Only isolates from the WHO priority specimens will be included. All reported isolates will be assessed for whether the WHO priority pathogen-antibiotic combinations were tested as per the WHO GLASS manual recommendations. Our secondary objective for this review will be:

1. To document if reporting of AST results is according to: “susceptible”, “intermediate” and “resistant” recommendations.

Search strategy

The following data bases will be searched: MEDLINE, SCOPUS, CINAHL and Embase. Key words used for the search will include: “Antimicrobial Resistance”, “Anti-microbial Susceptibility”, “AST”, “AMR Surveillance”, “Diagnostic”, “Africa” and specific names of all African countries, table 1. Finally, screening of reference lists of included documents for relevant articles will be undertaken. End note will be used to manage citations, and Covidence for screening abstracts and full texts and Excel (Microsoft Corporation) will be used for data extraction and charting stages of this review.

Table 1 provides sample search terms/concepts which will be searched as key words and subject headings.

MeSH search terms	“Drug resistance” OR “Antimicrobial resistance” OR “Bacterial resistance” OR “Drug Resistance, Bacterial", OR “Microbial Sensitivity Tests OR “Drug Resistance, Microbial” **AND**
text word search	text word search: “antibiotic resistan*” OR “antibacterial resistan*” OR “antimicrobial resistan*” OR “antimicrobial drug resistan*” OR “antibiotic drug resistan*” OR “antibacterial drug resistan*” OR “bacteraemia” OR “bacteremia” OR “bloodstream inf*” **AND**
title and abstract	“angola” OR “benin” OR “botswana” OR burkina faso” OR “burundi” OR “cameroon” OR “cape verde” OR “central african republic” OR “chad” OR “ivory coast” OR “cote d ivoire” OR “congo” OR “comoros” OR “djibouti” OR “Equatorial Guinea” OR “eritrea” OR “ethiopia” OR “gabon” OR “gambia” OR “ghana” OR “guinea” OR “guinea bissau” OR “kenya” OR “leshoto” OR liberia” OR “madagascar” OR”malawi” OR “Mali” OR “mauritania” OR “mozambique” OR “namibia” OR “niger” OR “nigeria” OR “rhodesia” OR “rwanda” OR “sao tome” OR “sengal” OR “seychelles” OR “sierra leone” OR “somalia” OR “south africa” OR “sudan” “swaziland” OR “tanzania” OR “togo” OR “uganda” OR “zambia” OR “zimbabwe” OR “africa”

Data extraction, charting, synthesis, analysis, and presentation of results

Following searching the primary sources, articles will be exported from Endnote into Covidence for further screening and analysis. Covidence will be used to remove duplicate sources from the initial pool and complete screening at 2 levels. We shall develop a template for data extraction. Key variables to be extracted will include: Author and year of publication, study title, inclusion criteria, study type, study setting, study population, priority specimen, priority pathogen, pathogens isolated/selected, antimicrobial agent/class used, reporting in the context of the WHO GLASS manual and significant findings.

The adapted extraction tool will be used in both the initial stages of study screening (to confirm study relevance) and selection and the later phase of data extraction from the selected studies. The customised data extraction tool will be used to collect relevant information on the (1) key study characteristics (e.g., publication year, publication type, study design, country, patient population characteristics) and (2) detailed information on the study context and population and (3) AST of bacterial isolates against the WHO GLASS recommendations.

To ensure systematic and reproducible study selection and data charting processes and to foster high inter-rater reliability, a calibration exercise will be undertaken. First, the review lead will use a seminal article to ascertain if the extraction instrument is appropriate for its intended use. Once confidence with the tool has been internally established, 2 members of the review team will be involved in the pilot of the extraction tool, using a minimum of twenty abstracts to review titles and abstracts against the above-mentioned inclusion criteria. We will review the results of the calibration, discuss any discrepancies among reviewers and make refinements to the extraction tool as identified and required. Reviewers will at the same time document reasons for exclusion on the extraction form and progress those articles considered relevant and eligible, to the second phase of full-text screening. Confirmed sources for inclusion in the scoping review will then be moved to the final stages of data extraction, charting, and synthesis.

Following the identification and selection of the relevant literature, we will explore within those studies, AST of isolates according to WHO GLASS pathogen-antibiotic combinations. The reviewers will independently chart data in duplicate from each eligible article. Should there be any disagreements among the reviewers, these will be resolved through discussion. The supervising reviewer will resolve any conflicts and provide oversight for the whole process. We aim to provide a descriptive summary of the gaps in implementation of the WHO GLASS manual, specifically to AST

based on the priority pathogen-antibiotic recommendation. Where relevant, we intend to suggest how the barriers can be addressed to improve AMR surveillance.

Risk of bias assessment or quality appraisal

Consistent with the JBI scoping review methodology and as this is a scoping review that aims to map all available knowledge regarding the study topic, we will not perform a risk of bias assessment. We shall appraise articles for quality using the CASP checklist. Where articles of low quality are included, a comment will be made.

Patient and public involvement

Patients and/or the public will not be directly involved in this study. However, the findings will be published with the wider community and policy makers with the view that they could be used to improve public health and contribute to efforts to control AMR.

Ethics and dissemination

No ethical clearance is needed for the current study as it will be based on already published articles. We will publish the findings of this study in international peer-reviewed journals and present them in conferences.

Results

The results of the study and the submission of a manuscript for peer review are expected in August 2024

Discussion

This proposed review is intended to map evidence of progress of implementing the WHO GLASS recommendations on AST for priority pathogen-antimicrobial combinations(15). It will inform current and future practices of AMR surveillance and provide ground for further research on GLASS implementation activity research and inform policy makers on areas of improvement in AMR control activities. Through conducting surveillance of specific pathogens over time, one can detect emerging pathogens and implement timely control, understand epidemiological trends, discover changes in the antimicrobial susceptibility profile of the organisms monitor, inform treatment guidelines and facilitate outbreak response(21, 22).

Conclusions

Antimicrobial resistance surveillance is one of the critical approaches to estimate and fight the burden of antibiotic resistance. This scoping review will be the first to provide information on the progress of implementation of the WHO GLASS initiative in Africa.

Acknowledgement

The authors would like to thank Wellcome Trust the funder of CAMO-Net Uganda Project.

Data availability

The data generated and analysed during this study will include content extracted from published, peer-reviewed journal articles. Full details about parameters and data sets will be reported in the scoping review publication

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

References

1. Murray CJL, Ikuta KS, Sharara F, Swetschinski L, Aguilar GR, Gray A, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. The Lancet. 2022;399(10325):629-55.
2. O'Neill J. Review on antimicrobial resistance. Antimicrobial resistance: tackling a crisis for the health and wealth of nations. 2014;2014(4).
3. World Health O. Global action plan on antimicrobial resistance. 2015.
4. World Health O. Antimicrobial resistance: global report on surveillance: World Health Organization; 2014.
5. de Kraker MEA, Stewardson AJ, Harbarth S. Will 10 million people die a year due to antimicrobial resistance by 2050? PLoS medicine. 2016;13(11):e1002184.
6. Hay SI, Rao PC, Dolecek C, Day NPJ, Stergachis A, Lopez AD, Murray CJL. Measuring and

mapping the global burden of antimicrobial resistance. BMC medicine. 2018;16(1):1-3.

7. Shankar PR, Balasubramanium R. Antimicrobial resistance: global report on surveillance 2014. Australasian Medical Journal (Online). 2014;7(5):237.

8. Jonas OB, Irwin A, Berthe FCJ, Le Gall FG, Marquez PV. Drug-resistant infections: a threat to our economic future (Vol. 2): final report. HNP/Agriculture Global Antimicrobial Resistance Initiative. 2017.

9. Seale AC, Hutchison C, Fernandes S, Stoesser N, Kelly H, Lowe B, et al. Supporting surveillance capacity for antimicrobial resistance: laboratory capacity strengthening for drug resistant infections in low and middle income countries. Wellcome open research. 2017;2.

10. Ashley EA, Recht J, Chua A, Dance D, Dhorda M, Thomas N, et al. Antimicrobial resistance in low and middle income countries. An Analysis of Surveillance Networks; IDDO: Oxford, UK. 2016.

11. Sulis G, Sayood S, Gandra S. Antimicrobial resistance in low-and middle-income countries: current status and future directions. Expert review of anti-infective therapy. 2022;20(2):147-60.

12. Kariuki S, Kering K, Wairimu C, Onsare R, Mbae C. Antimicrobial resistance rates and surveillance in sub-Saharan Africa: where are we now? Infection and drug resistance. 2022:3589-609.

13. Nadimpalli M, Delarocque-Astagneau E, Love DC, Price LB, Huynh B-T, Collard J-M, et al. Combating global antibiotic resistance: emerging one health concerns in lower-and middle-income countries. Clinical Infectious Diseases. 2018;66(6):963-9.

14. Van Boeckel TP, Pires J, Silvester R, Zhao C, Song J, Criscuolo NG, et al. Global trends in antimicrobial resistance in animals in low-and middle-income countries. Science. 2019;365(6459):eaaw1944.

15. World Health O. Global antimicrobial resistance surveillance system: manual for early implementation: World Health Organization; 2015.

16. World Health O. Comprehensive Review of the WHO Global Action Plan on Antimicrobial Resistance. 2021.

17. World Health O. Global antimicrobial resistance and use surveillance system (GLASS) report: 2021. 2021.

18. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. International journal of social research methodology. 2005;8(1):19-32.

19. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA extension for

scoping reviews (PRISMA-ScR): checklist and explanation. Annals of internal medicine. 2018;169(7):467-73.

20. Peters MDJ, Marnie C, Tricco AC, Pollock D, Munn Z, Alexander L, et al. Updated methodological guidance for the conduct of scoping reviews. JBI evidence synthesis. 2020;18(10):2119-26.

21. Fuhrmeister AS, Jones RN, editors. The importance of antimicrobial resistance monitoring worldwide and the origins of SENTRY antimicrobial surveillance program2019: Oxford University Press US.

22. Diallo OO, Baron SA, Abat C, Colson P, Chaudet H, Rolain J-M. Antibiotic resistance surveillance systems: A review. Journal of Global Antimicrobial Resistance. 2020;23:430-8.