Protocol of the scoping review – Highest priority critically important antimicrobials resistance in food producing animals in Africa

This protocol used the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P) as a guideline (Moher *et al*., 2015). The PRISMA-P was developed specifically for systematic reviews therefore, certain components had to be adapted for this scoping review.

ADMINISTRATIVE INFORMATION

Title

A scoping review on the Highest priority critically important antimicrobials resistance in food producing animals in Africa

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Contributions

Contribution	**Authors**
Concept idea	VN, LC
Drafting protocol	VN, MJ, MF, LC
Defining eligibility criteria	All
Search strategy	VN
Search verification	VN, LC
Title and abstract screening	AA, MJ, VN, WM
Full-text screening	AA, MJ, VN, WM
Data extraction	AA, VN, MF, WM, LC
Data analysis and synthesis of results	AA,VN, MF, MJ, MM, WM, LC
Drafting paper	AA, VN, MF
Reviewing paper	GS, MM, LC

Support
This project have not be funded.

INTRODUCTION

Rationale (3)

Antimicrobial resistance (AMR) is a serious public health concern and one of the most important health challenges in the 21st century that requires action across all government sectors and society (FDA, 2020; Tarakdjian *et al*., 2020). A recent review estimated that the death rate attributable to AMR was highest in African regions (Murray *et al*., 2022). The AMR situation in Africa is compounded by several factors, including lack of access to appropriate antimicrobial therapy, limited regulations to control the use of antimicrobials in human and veterinary medicine, limited/lack of surveillance systems, lack of infrastructural and institutional capacities, inadequate use of antimicrobials, and lack of treatment guidelines (Ngom *et al.,* 2017; Mouiche *et al.,* 2018; Elton *et al.,* 2020).

AMR has a complex epidemiology. Resistant bacteria can be transmitted across species and ecosystems. It is well known that antimicrobial use (AMU) is the main driver of AMR

(Dutra *et al*., 2021). About 73% of all antimicrobials sold worldwide are used in livestock production. From these more than two thirds are reported for use in poultry, pigs and cattle (Van Boeckel *et al*., 2017; FAOSTAT, 2021). In addition, Tiseo *et al*. (2020) estimated that between 2010 and 2030, the global consumption of antimicrobials will increase by 67%, with a third of the increase in livestock imputable to shifting production practices in middle-income countries.

The use of antimicrobials for livestock production raises concerns about the emergence and selection of resistant bacteria within these systems. Resistant bacteria could afterwards be transmitted to humans leading to a negative impact in population health and the economy (De Oliveira *et al*., 2020; Dutra *et al.,* 2021). Evidence indicates that a reduction in AMU in animal husbandry would lead to a decrease in AMR levels (WHO, 2017).

Measures to reduce AMU in animal production are particularly stringent with the use of highest critically important antimicrobials (HPCIAs) (Diana *et al*., 2021). Due to their importance for the treatment of specific infections in humans, the use of HPCIAs in food producing animals should be restricted to particular cases, according to strict indication criteria, in order to minimize AMR development (WHO, 2018). Following this recommendation, several developed countries have taken steps to reduce HPCIAs usage in production animals (Trauffler *et al*., 2014; Obritzhauser *et al*., 2016; Diana *et al*., 2021; Ngom *et al*., 2022). However, little is known about African countries. Previous systematic reviews on AMU and resistance in food producing animals in Africa indicated a large deficit of data on HPCIAs usage and resistance (Cuong *et al*., 2018; Kimera *et al*., 2020). Summarize available information on HPCIAs resistance in Africa is for great importance for policies and mitigation strategies to reduce the public health risk of AMR. To the best of our knowledge, this will be the first scoping review focused on HPCIAs resistance in livestock production in Africa.

Objectives (4)

This protocol defines the methodology to review and summarize the available information on HPCIAs resistance in livestock production (poultry, cattle, pigs, goats and sheep) in Africa to better inform future policies aiming to control AMR in the food production chain.

This scoping review has the following objectives:

- To identify and describe the existing literature on HPCIAs resistance (prevalence and genotyping) in food-producing animals in Africa;
- To identify and discuss any research gaps within this topic.

The specific PICo elements are:

1. **P**opulation: poultry, cattle, pigs, goats and sheep
2. **I**nterest: *Escherichia coli, Salmonella* spp, *Campylocater* spp, *Staphylococcus aureus; Enteroccocus* spp resistant to HPCIAs
3. **Co**ntext: African countries

METHODS

Protocol and Registration (5)

This protocol is archived at the Veterinary Public Health Institute of University of Bern in Switzerland website and published online with Systematic Reviews for Animals and Food (SYREAF) available at: http://www.syreaf.org/.

Eligibility criteria (6)

Inclusion critedia

1. Criteria related with the elements of the PICo question (Population, Interest and Context).
2. Language: Publications in English and French.
3. Publication types: Journal articles reporting original research data, fulfills the study design eligibility criteria (cross-sectional, longitudinal study, case-control study, cohort study)
4. Publication date: 2001 to 2021 because according to previous reviews on AMR in Africa, most of the studies were carried out after 2010 (Mouiche *et al*., 2019; Kimera *et al.*, 2020; Kivumbi et Standley, 2021).
5. Geographical location of studies: African countries
6. Availability of full-text article

Exlusion criteria

1. Studies reporting aggregated data such as studies with the methodology or results aggregating resistance rates in a large category such as 'Gram-negative organisms', Gram-positive organisms or 'Enterobacteriaceae' or bacteria selected (*Escherichia coli, Salmonella* spp, *Campylocater* spp, *Staphylococcus aureus; Streptococcus pneumoniae; Enteroccocus* spp) with others bacteria.
2. Studies without information on total bacteria isolates
3. Studies reporting aggregated data on HPCIAs and non HPCIAs resistance

Information sources (7)

To identify potentially relevant documents, the search will be conducted in four databases: CAB abstract (OVID interface), Web of Science (WOS), and PubMed available via the University of Bern (Switzerland) and African Journals Online databases.

All the databases of WOS will be used (Web of science core collection, BIOSIS Citation Index, KCI-Korean Journal Database, Medline, Russian Science Citation Index and SciELO Citation Index). However, we will exclude the following editions: Arts & Humanities Citation Index (A&HCI), Conference Proceedings Citation Index-Science (CPCI-S), Conference Proceedings Citation Index-Social Science & Humanities (CPCI-SSH) and Social Sciences Citation Index (SSCI).

As a search validation procedure, we will scan the reference lists of relevant review papers on this topic. Relevant articles found will be treated in an identical manner to those found during the initial database search.

Search (8)

The search terms will be the same for all databases, but the formatting of the terms will vary due to different architectures in the databases (see supplement). If applicable, search terms will include subject heading search, such as Medical Subject Headings (MeSH) from Pubmed. The concept of the search strategy will be the following:

[**HPCIAs**] AND [**resistance or resistant or susceptibility**] AND [**cattle or poultry or pig or sheep or goat**] AND [**African countries**].

The general search strategy to identify studies relevant to the PICo of this review will be the following:

#1 ("highest priority critically important antimicrobial" or HPCIA or HP-CIA or ketolide or cephalosporin or cefcapene or cefdaloxime or cefdinir or cefetamet or cefixime or cefmenoxime or cefodizine or cefotaxime or cefovecin or cefpimizole or cefpodoxime or cefteram or ceftibuten or ceftiofur or ceftiolene or ceftizoxime or ceftriaxone or cefoperazone or ceftazidime or oxacephems or quinolone or Levofloxacin or ciprofloxacin or norfloxacin or danofloxacin or eurofloxacin or moxifloxacin or ofloxacin or norfloxacin or marbofloxacin or gemifloxacin or enoxacin or lomefloxacin or sparfloxacin or gatifloxacin or polymyxin or

macrolide or tilmicosin or erythromycin or spiramycin or tulathromycin or glycopeptide or colistin or tylosin or vancomycine or teicoplanine)

#2 (resistance or resistant or susceptibility or susceptible)

#3 (pig* or swine* or pig* or weaner or fattener or sow or piglet* or boar or boars or "*Sus domesticus*" or chick* or poultry* or broiler* or layer* or turkey* or duck* or geese or goose or fowl* or avian* or egg or eggs or bird* or hen or hens or "gallus gallus" or flock* or cattle or beef or cow* or calf or calves or "Bos indicus" or heifer* or bull* or bovine or dairy or zebu or sheep* or caprine or goat* or ovine or ewe, or "small ruminant" or "food-producing animal*" or "food animal*" or " animal husbandry" or "animal farming" or "domestic animal*" or livestock)

#4 (Africa or African or Comoros or Djibouti or Madagascar or Malawi or Seychelles or Cameroon or "Central African Republic" or Chad or Congo or "Equatorial Guinea" or "Atlantic Islands" or Gabon or Morocco or Sudan or Botswana or Lesotho or Swaziland or Benin or "Burkina Faso" or "Cape Verde" or Ghana or Guinea or Mauritania or Niger or Senegal or "Sierra Leone" or Togo or Burundi or Eritrea or Ethiopia or Kenya or Mozambique or Rwanda or Somalia or Tanzania or Uganda or Zambia or Zimbabwe or Angola or Algeria or Egypt or Tunisia or Namibia or "South Africa" or Gambia or Liberia or Mali or Nigeria or "Ivory Cost")

#1 AND #2 AND #3 AND #4

The final search strategy for WOS can be found in Additional file 1.

Selection of Sources of Evidence (9)

All citations retrieved in the literature search will be imported into Zotero and deduplication will be carried out using the de-duplication process.

After duplicate removal, the file obtained will be uploaded to Rayyan to facilitate collaboration among reviewers during the study selection process. Indeed, three independent reviewers will perform the screening at each stage of the review to reduce the possibility of excluding relevant reports. Half of the citation will be assigned to two authors (MJ et WM) and the other half to two others author (VN and AA) will screen all the papers. This will guarantee that each reference is screened by two independent reviewers.

The manusccripts will be screened in two independent stages. To increase consistency among reviewers, at each stage, the three reviewers will screen the first 20 publications, discuss and amend the results before beginning the screening process. This calibration exercise will enable discussion and solve disagreements before carrying out the full selection process (Windeyer *et al*., 2021).

In the first stage of the selection process all the reviewers will screen the titles and abstracts. Disagreements on study selection will be resolved by consensus and discussion with other reviewers if needed (Duffett *et al*., 2013).

Eligibility of studies will be assessed with the following questions:

1. Is the abstract of the study available? YES [INCLUDE], NO [EXCLUDE]
2. Does the study concern bacterial resistant to antibiotics? YES [INCLUDE], NO [EXCLUDE], UNCLEAR [INCLUDE]
3. Does the study concern at least one of the following species: poultry, cattle, pig, sheep, goat? YES [INCLUDE], NO [EXCLUDE], UNCLEAR [INCLUDE]
4. Is the study original research? YES [INCLUDE], NO [EXCLUDE], UNCLEAR [INCLUDE]
5. Does the study take place in at least one Africa country? YES [INCLUDE], NO [EXCLUDE] UNCLEAR [INCLUDE]

Full text screening will be performed for the papers that met the inclusion criteria in the first phase.

Eligibility of studies will be assessed with the following questions:

1. Is a full text available? YES [INCLUDE], NO [EXCLUDE]
2. Is the full text available in English or French? YES [INCLUDE], NO [EXCLUDE]
3. Does the sudy concerned at least one of these bacteria *Escherichia coli, Salmonella* spp, *Campylocater* spp, *Staphylococcus aureus; Enteroccocus* spp YES [INCLUDE], NO [EXCLUDE]
4. Does the study concern bacterial resistant to at least one HPCIAs? YES [INCLUDE], NO [EXCLUDE]

Data Charting Process (10)

To ensure consistency across reviewers, reviewers will conduct a calibration exercise using five randomly selected papers before starting the data charting process. Two reviewers will

independently extract data by using a pre-defined table created in Excel. This data-charting form will be jointly developed by all the authors. The two reviewers will independently chart the data, discuss the results and continuously update the data charting form in an iterative process (Lenzen *et al*., 2017). Disagreements for which a consensus cannot be found will be resolved by a third reviewer. Data extracted will include demographic information, methodology, and others details described below. We will contact study authors to resolve any uncertainties if necessary.

Data items (11)

Data to be extracted from eligible studies will include the following items:

General information

- First author
- Year of publication
- Duration of study
- Country of study (where the study was conducted). If not stated, contact study authors or use NA if the author didn't reply
- Sub-region of study (Eastern, Western, Northern, Middle and sub-Saharan Africa)
- Study design (cross-sectional, longitudinal study, etc.)

Population data

- Animal production type: level 1 (species), cattle, poultry, swine, sheep, goat, at least two species combined; level 2, beef cattle, dairy cattle, calves, heifers, broilers, layer chickens, turkeys, weaners, finishing pigs, adult pig/sows, etc.
- Number of farms or animals used in analysis
- Sampling point (farm, slaughterhouse, retail market, etc.)
- Sample type (faeces, meat, milk, blood, egg, etc.)
- Sample size
- Number of specimens collected

Interest data

- Antimicrobial susceptibility testing methodology
- Bacteria of interest (*Escherichia coli, Salmonella* spp, *Campylocater* spp, *Staphylococcus aureus; Enteroccocus* spp, etc.)

- HPCIAs to which bacteria of interest are resistant
- Proportion of antibiotic-resistant bacteria
- AMR genes analyzed
- Methodology used for molecular analysis

It is important to note that intermediate-resistant samples will be recorded as resistant in this study (Ahmed *et al*., 2019).

Synthesis of Results (12)

The results of the literature search will be reported, including numbers of citations screened, duplicates removed, and full-text documents screened. A flow diagram that details the reasons for exclusion at the full-text level of screening will also be provided. A narrative synthesis will be provided with information presented as text, diagrams, and maps. Tables to summarize and explain the characteristics, findings and research gaps of the included studies will also be used. Results expressed as a range of the proportion of resistance will be presented according to the country, sub-region, bacteria species, animal origin, resistance patterns, HPCIAs, virulence, etc. If not defined by the study, resistance to three or more antibiotics, frequently used in the primary reports, will be considered as multidrug resistance (MDR).

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