

Protocol of the scoping review – Public health risk assessments of antimicrobial resistance from poultry, cattle and pig

This protocol used the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols extension for Scoping Reviews (PRISMA-ScR) as a guideline (Tricco et al., 2018).

ADMINISTRATIVE INFORMATION

Title

A scoping review on the use of risk assessment methodology to evaluate public health risks of antimicrobial resistant bacteria from poultry, cattle and pig

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Contributions

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

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INTRODUCTION

Rationale (3)

Antimicrobial resistance (AMR) is a serious public health concern and one of the most important health challenges in the 21st century (FDA, 2020; Tarakdjian *et al.*, 2020). AMR has a complex epidemiology and resistant bacteria can be transmitted across species and ecosystems. It is known that antimicrobial use is the main driver of AMR. The use of antimicrobials for livestock production raises concerns about the emergence and selection of resistant bacteria within these systems that can afterwards be transmitted to humans associated with increased impact in population health and economy (De Oliveira *et al.*, 2020; Dutra *et al.*, 2021).

Current approaches to understanding the risks associated with AMR include the use of risk assessments (RA) methods. Due to increasing threats and decreasing financial resources, risk ranking method is also used, to rank by level of importance, the risk to public health (PH) related to AMR to enable decision makers to focus on the most important hazards (Stella *et al.*, 2013; Devleeschauwer *et al.*, 2017). Food animal production rapidly expands, as well as the antimicrobial use and AMR (Hedman *et al.*, 2020). For example, antibiotic consumption in poultry is expected to increase by 143% from 2010 to 2030 (Van Boeckel *et al.*, 2015).

Snary *et al.* (2004) reviewed microbial risk assessments applied to the area of AMR. Their review included a summary of the key data limitations/issues affecting microbial risk assessment applied to AMR at that time. Recently, Caffrey *et al.* (2019) published a scoping review, which aimed at identifying and describing the literature on risk assessments for the study of AMR of foodborne bacteria in humans, with focus only on products intended for the treatment of bacterial infections. This review selected the studies with all the four steps of RA methodology. Yet, because of the robustness of the data needed to complete a RA study, only few studies have been conducted with all the steps of the RA methodology. However, more studies limited on only one or two of those steps.

It is of relevance to understand the scientific evidence available and how this potential PH risk has been systematically evaluated.

Objectives (4)

This scoping review has the following objectives:

- To identify and describe the existing literature that used RA methods to evaluate the public health risk related to AMR bacteria from poultry, cattle and pig;
- To identify and discuss any research gaps within this topic in relation to RA methodologies.

This proposed scoping review will answer the following questions:

- What literature has been published which describes public health RA of AMR from poultry, cattle and pig?
- How RA were used with respect to the PH risk of AMR from poultry, cattle and pig?
- What were the conclusion of the RA with respect to the PH risk of AMR from poultry, cattle and pig?

This study focus on poultry, cattle and pig because the majority of antimicrobial are used in these livestock species (Tiseo *et al.*, 2020) which account for more than 90% of all foodstuffs of animal origin consumed worldwide (FAOSTAT, 2021).

Table 1: PICo of the study

P (Population/problem)	Antimicrobial resistant for PH
I (Interest)	Use of risk assessment methods
Co (Context)	poultry, cattle and pig production

METHODS

Protocol and Registration (5)

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

Eligibility criteria (6)

Inclusion criteria of this study are defined based on the PICO (Problem, Interest, and Context) as presented in the table 1. Of interest are studies addressing public health risk assessment related to AMR bacteria from poultry, cattle and pig. Human health risk assessment objective is to estimate the probability and amplitude of illness and deaths caused by the infection associated with AMR bacteria or determinants acquired from poultry, cattle and pig products after transmission or development through food consumption or contact between humans and their products. We will include studies examining bacteria resistance to antibiotics from poultry, cattle and pig (included eggs, meat, etc.) along the production/supply chain (i.e., in the farm, slaughterhouse, industries, market/shop or household/restaurant). We will exclude studies on resistance viruses, protozoal, fungal, parasites, mycobacterium. We anticipate that the volume of studies describing all the four core elements (Ben *et al.*, 2019) of RA (hazard identification, exposure assessment, hazard characterization, and risk characterization) in the same paper will be limited. Thus, qualitative, quantitative and mixed-method studies with at least one step of the RA methodology will be considered in order to consider different aspects of measuring PH impact. Studies selected will not be limited by the study design, the type of RA methodology and adverse health outcomes used (number of death, sick, treatment failure, disability-adjusted life-years, healthy life expectancy, loss of treatment option, increased severity of infections manifested by prolonged duration of disease, etc.). Though the terms used in the search strategy are in English, no limits are placed on publication language. The search will not be limited based on the date of publication, and geographical location. We will only consider original studies. Gray literature (report, proceeding, review, thesis, etc.) will be excluded.

Information sources (7)

To identify potentially relevant documents, the search will be conducted in three databases via the University of Bern (Switzerland): CAB Abstracts (OVID interface, 1973 onwards to date of search), MEDLINE (OVID interface, 1946 onwards to date of search), and Web of Science

(1900 onwards to date of search). These databases are selected to provide a high level of article recall across biomedical articles (Bramer *et al.*, 2017). In Web of Science, we will use all databases (Web of science core collection, BIOSIS Citation Index, KCI-Korean Journal Database, Medline, Russian Science Citation Index and SciELO Citation Index). But for the Web of science core collection, 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). To ensure literature saturation if necessary, we will scan the reference lists of studies included after full text screening and relevant reviews and meta analysis in this topic. Scopus (1961 onwards to date of search) and Google Scholar will be used for this backward searching. Articles found will be treated in an identical manner to those found during the initial database search.

Search (8)

Search terms (table 2) will be combined using the boolean operators and for the following three themes: AMR bacteria, risk assessment, and poultry, cattle and pig. The search terms will be the same for all databases, but the formatting of the terms will vary due to different architectures in those databases (see supplement). If applicable, search terms will include Medical Subject Headings (MeSH), Thesaurus, truncation and wildcards. Details of the search strategy in each database are provided in the supplement materials.

Table 2:

	Problem	Interest	Context
	AMR Risk of antimicrobial resistant for PH	Risk assessment/ranking Use of risk assessment methodology	poultry, cattle and pig (include meat and eggs)
Mesh term	Drug resistance	Risk assessment	Poultry, pig, Cattle
Search terms	("Methicillin-resistant Staphylococcus aureus" or "Carbapenem-resistant Enterobacterales" or "Vancomycin-resistant enterococci" or "Extended-spectrum β -lactamases" or "Carbapenem-resistant-Escherichia" or "Vancomycin-resistant enterococcus" or "Extended-spectrum beta-lactamases" or MRSA ¹ or CRE ² or VRE ³ or ESBL ⁴) or ((drug or multidrug or MDR or antibiotic or antimicrobial or microbial or antibacterial or bacterial or carbapenem* or cephalosporin* or vancomycin* or methicillin* or *quinolone* or ampicillin* or macrolide* or tetracycline* or penicillin* or colistin* or tylosin*) and (resistance or resistant))	"Risk assessment" or "Risk scoring" or "Risk management" or "Risk model" or "Risk study" or "Risk analysis" or "Risk characterization" or "Risk estimation" or "Risk ranking" or "Hazard identification" or "Hazard analysis" or "Hazard characterization" or "Exposure assessment" or "release assessment" or "dose-response assessment" or "consequence assessment" or "health risk" or "exposure pathway" or "release pathway" or "human exposure"	"food animals" or livestock or "domestic animal" or meat or chick* or broiler* or turkey* or duck* or geese or goose or fowl* or avian* or eggs or bird* or hen* or cattle or beef or cow or calf or calves or bos or heifer* or bull* or bovine or dairy or zebu or swine or pig* or piglet* or pork*

Key articles were identified by principal Investigator and keywords were mined by finding references in the selected databases. The key articles are below:

- Alban, L., Nielsen, E. O., & Dahl, J. (2008). A human health risk assessment for macrolide-resistant *Campylobacter* associated with the use of macrolides in Danish pig production. *Preventive veterinary medicine*, 83(2), 115-129.

- Alban, L., Ellis-Iversen, J., Andreasen, M., Dahl, J., & Sönksen, U. W. (2017). Assessment of the risk to public health due to use of antimicrobials in pigs—an example of pleuromutilins in Denmark. *Frontiers in veterinary science*, 4, 74.

¹ MRSA: Methicillin-resistant *Staphylococcus aureus*

² CRE: Carbapenem-resistant *Enterobacterales*

³ VRE: *Vancomycin-resistant enterococci*

⁴ ESBL: Extended-spectrum β -lactamases

- Anderson, S. A., Woo, R. Y., & Crawford, L. M. (2001). Risk assessment of the impact on human health of resistant *Campylobacter jejuni* from fluoroquinolone use in beef cattle. *Food Control*, 12(1), 13-25.

- Doménech, E., Jiménez-Belenguer, A., Pérez, R., Ferrús, M. A., & Escriche, I. (2015). Risk characterization of antimicrobial resistance of *Salmonella* in meat products. *Food control*, 57, 18-23.

- Hurd, H. S., Doores, S., Hayes, D., Mathew, A., Maurer, J., Silley, P., ... & Jones, R. N. (2004). Public health consequences of macrolide use in food animals: a deterministic risk assessment. *Journal of food protection*, 67(5), 980-992.

Selection of Sources of Evidence (9)

All citations found in the literature search will be imported by the main author into a free web based reference management software (Zotero). De-duplication will be carried out using the de-duplication process by juxtaposing author names, date of publication and title of the article.

After duplicate removal, the file obtained will be uploaded to Rayyan data management software 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 assign to one author, the third author will review all the papers excluded by the two others.

To increase consistency among reviewers, the three reviewers will screened the 1/100 of publications, discussed the results and amended the screening before beginning screening for this review. A second calibration exercise will be done if a 70-80% level of agreement is not reached. The review authors will independently screen the titles and abstracts yielded by the search according to the criteria described in table 3. DeepL website will be used for translation if needed. The references will then be allocated to one of two categories and placed in the corresponding category of the database:

- Relevant or uncertain if relevant for this study: the reference is included;
- Not relevant for this study: the reference was determined to be out of scope.

Table 3: Guideline for relevance screening

	Question	Answer options	Included	Excluded
1	Does the study concern resistant bacteria or resistance determinants from bacteria?	Yes or unsure		
		No		viruses, parasites, mycobacterium, fungal, etc.
2	Does the paper describe a risk assessment procedure or part of it (hazard identification, exposure assessment, hazard characterization and risk characterization) related to public health?	Yes or unsure		
		No		
3	Is the resistant bacteria or resistance determinants from bacteria are from on poultry, cattle pig, included eggs, and cattle milk and cattle/pig or poultry by-products?	Yes or unsure		
		No		Others animals (goat, sheep, etc.) and their by-products (i.e. goat or sheep milk)

For each half of the references, once both reviewers will screen the sampled articles by title and abstract, the conclusion on whether to include or exclude will be compared in order to measure the inter-rater reliability using observed proportional agreement and Cohen’s kappa, calculated manually using the method described below (Cohen, 1960). Disagreements will be resolved by consensus or third-party consultation (LPC) when consensus will not be achieved.

		Reviewer 1	
		Include	Exclude
Reviewer 2	Include	a	b
	Exclude	c	e

Proportional agreement =

$$p_o = \frac{a + d}{a + b + c + d}$$

Probability of yes at random =

$$p_{yes} = \frac{a + b}{a + b + c + d} \cdot \frac{a + c}{a + b + c + d}$$

Probability of no at random =

$$p_{no} = \frac{c + d}{a + b + c + d} \cdot \frac{b + d}{a + b + c + d}$$

Overall random agreement probability =

$$p_e = p_{yes} + p_{no}$$

Cohen's kappa =

$$k = \frac{p_o - p_e}{1 - p_e}$$

After the title and abstract screening, a full text screening in the relevant or uncertain group for selecting studies for final inclusion will be performed by both reviewers. References without full text will be automatically excluded.

Data Charting Process (10)

To ensure consistency across reviewers, the three reviewers will conduct calibration exercises before starting data charting by using the first five papers selected. A similar approach used during screening process will be applied (Martin-Misener *et al.*, 2012). After guaranteeing that everything is fine and the required adaptations are made, the reviewers will then performed data extraction of each of articles meeting eligibility criteria. Each reviewer will extract data independently and reported into a Microsoft Excel form (supplementary materials). This data charting form was created by RVN based of four references papers that would certainly be include in our review (Hurd *et al.*, 2004; Doménech *et al.*, 2015; Alban *et al.*, 2017; Collineau *et al.*, 2018). This data-charting form which consider data related to the four core elements of risk assessment will be validated by all the reviewers during calibration exercise but as charting the results will be an iterative process, whereby the charting table will be continually updated.

Extracted data will include demographic information, methodology details, and all reported outcomes related to PH. As at the previous stage, reviewers will resolve disagreements by consensus or third-party arbitration (LPC). The main data that will be extracted in final included articles are: first author's name, year of publication, study design (eg, randomised trial, non-randomised trial, cross-sectional design, or pre-post study), country/region to which the RA pertains to, study area (city, regional, national, international, etc.), source of the hazard (meat, eggs, etc.), place of collection of the source of hazard (household, farm, slaughterhouse, etc.), resistant bacteria species, resistant determinant, antibiotic agent to which resistance is expressed, population at risk (adult, children, females, etc.), route of exposure (consumption, etc.), outcomes identified (infection, treatment failure, number of death, disability-adjusted life-years, healthy life expectancy, etc.), modelling approach to evaluated the risk (odd ratio,

prevalence, incidence, etc.), RA data (qualitative, or quantitative, mixed), and type of RA method used (Codex Alimentarius or OIE), etc.

Data items (11)

Data items to be extracted from the final selection of full texts have been described above. But more details on these information is also available in the "Data extraction form" presented as an annex.

Critical Appraisal of Individual Sources of Evidence (12)

Not applicable.

Summary Measures (13)

Not applicable.

Synthesis of Results (14)

A narrative synthesis will be provided with information presented in the text and tables to summarize and explain the characteristics, findings and research gaps of the included studies. The narrative synthesis will explore the relationship and findings both within and between the included studies, in line with the RA methods used. Results will be presented according to the different steps of the RA methods.

Risk of bias Across Studies (15)

Not applicable.

Additional Analyses (16)

Not applicable.

Discussion

This scoping review will provide a synthesis of the current gaps on the use of RA methodologies for PH impact related to AMR from food of animal origin (related to poultry, pig and cattle species). Results of this review will be very helpful for researchers and policy makers to improve RA.

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