

Exploring Antimicrobial Resistance in *Escherichia coli*: A Scoping Review Protocol Comparing Antibiotic-free and Conventionally Raised Beef Cattle in North America

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Registrations

The protocol will be archived in PRISM: University of Calgary Digital Repository (<http://prism.ucalgary.ca>) and published online with Scoping Reviews for Animals and Food (<http://syreaf.org>). The protocol will follow Prisma ScR guidelines for Scoping Reviews[1].

Support

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Amendments

Protocol deviations will be documented in case amendments are done after its registration.

INTRODUCTION

Abstract

Escherichia coli is a gram-negative bacterium commonly found in the human and animal gastrointestinal tract. Beef cattle are considered reservoirs, although some strains can trigger diarrhea in newborn calves. Certain strains, such as Shiga toxin-producing *E. coli* (STECs), pose health risks in humans and animals [2]. Antibiotic resistance in *E. coli* is a significant concern in human and veterinary medicine, as it can lead to treatment challenges and transmission to other bacteria [3]. Canada and the United States Drug-Resistant Index score lie among the lowest ten countries, and this can be associated with the wide use of narrow-spectrum penicillin [4]. Strains encode accessory resistance and are likely resistant to multiple antibiotic classes [5]. Evidence suggests that *E. coli* can be resistant to more than one antimicrobial drug, and the most common resistance phenotypes are older drugs such as tetracycline, sulfonamide, streptomycin, and ampicillin [6]. Antibiotic-free beef cattle certifications have been implemented to address antimicrobial resistance concerns in the food chain [7]. However, the evidence regarding the prevalence of resistant bacteria in antibiotic-free production systems is limited. Antimicrobial resistance in *Escherichia coli* represents a significant One Health issue, highlighting the urgent need to explore alternatives, such as limiting the use of antibiotics in beef cattle production to therapeutic treatments, to mitigate the spread of resistant strains and safeguard human and animal health [8].

Objectives

The objective of this study is to lead a scoping review to define the range of existing research in the area, individualize research gaps and suggest areas important for future research studies about Antimicrobial Resistance in *Escherichia coli* of Antibiotic-free and Conventionally Raised Beef Cattle from North America.

Methods

This scoping review has been designed following the JBI Reviewer's Manual [9] and the PRISMA ScR guidelines for scoping reviews [1] to report it and the search question was constructed using the PICO framework. We will search the literature for peer-reviewed articles using the following databases: CAB Abstracts, BIOSIS Previews, Environmental Complete, the Web of Science's Science Citation Index and Emerging Sources Citation Index. The grey literature search will include a search of ProQuest Dissertations and the websites of relevant government departments, agencies, and industry groups. Two independent reviewers will screen the articles at the title, abstract, and full-text levels.

METHODS

This scoping review has been designed following the JBI Reviewer’s Manual [9] and the PRISMA ScR guidelines for scoping reviews [1] to report it.

The search question is outlined below using the PICO framework (Population, Intervention, Comparator, Outcomes) [10].

POPULATION (P)	Beef cattle and sub-products
INTERVENTION/ EXPOSURE (I)	Antibiotic-free (including organic, Verified Grass-Fed, Raised Without the Use of Antibiotics, RWA, and Verified Natural Beef)
COMPARATOR (C)	Conventionally raised beef cattle
OUTCOME (O)	An occurrence of antimicrobial-resistant <i>E. coli</i> from faecal, the environment, and meat samples

Information sources

We will search the literature for peer-reviewed articles using the following databases: CAB Abstracts, BIOSIS Previews, Environmental Complete, the Web of Science’s Science Citation Index and Emerging Sources Citation Index. Articles should be full text available in English. The search will include keywords and controlled vocabulary terms for the following concepts: beef cattle, *E. coli*, microbial resistance, organic farming, and related terms such as ‘raised without.’ A complete CAB search strategy is attached as Appendix A. This search will be translated into the vocabulary and syntax of the other databases.

The grey literature search will include a search of ProQuest Dissertations and the websites of relevant government departments, agencies, and industry groups.

A librarian (HG) will conduct the literature search and import eligible results into Covidence [11].

References from articles identified either through the librarian search or the grey literature search will be reviewed. Appropriate studies will be inserted manually into Covidence.

Review question

What is the evidence of a difference in the occurrence of antimicrobial-resistant *Escherichia coli* of antibiotic-free and conventionally raised beef cattle from North America?

Eligibility criteria

Inclusion Criteria

BEEF PRODUCTION	SAMPLES	PRODUCTION UNIT	PUBLICATION SOURCE
<ul style="list-style-type: none"> • Entire beef production continuum 	<ul style="list-style-type: none"> • Faecal • Meat: <ul style="list-style-type: none"> - Abattoirs - Slaughterhouses - Retail Beef • Environmental: <ul style="list-style-type: none"> - Soil - Manure - Air - Water - Facilities 	<ul style="list-style-type: none"> • Organic Beef (CFIA-Canada) • USDA Organic (USA) • Verified GrassFed (USDA certified) • Raised without the use of antibiotics (CFIA-Canada) • Raised without antibiotics/RWA (NSF- USA) • Verified Natural Beef (IMI Global-USA) 	<ul style="list-style-type: none"> • Published in a peer-reviewed journal • Grey literature: Published in a governmental site

The inclusion criteria have been categorized into four sections (beef production, origin of *E.coli* samples, production unit and publication source). Articles should contain at least one item of each category to be considered part of this study, and articles that compare one of the stated production units with conventionally raised cattle will also be included. Term variations will be accepted.

Exclusion Criteria

LANGUAGE	PRODUCTION UNIT
<ul style="list-style-type: none"> • Full-text is not available in English 	<ul style="list-style-type: none"> • Natural meat (Canada) • Grass-fed (Canada) • Cull cows from the dairy industry

Study records

Data management

Studies will undergo two phases in the screening using Covidence. Two independent reviewers will conduct data in both screening phases (VMS) and (WBD). Disagreements will be resolved by another independent reviewer (SC).

First phase

The first phase will focus on the title and abstract screening.

- Is there a full text available in English?
- Does the title or abstract mention or refer to a primary research study published in a peer-reviewed journal?
- Does the title or abstract suggest an involvement of resistant *E. coli* from antibiotic-free or antibiotic-free and conventional beef cattle production chains?

The possible answers to those questions are 'yes,' 'no,' or 'uncertain.' Articles classified as 'no' by both reviewers will be excluded. Articles classified as 'yes' by both reviewers will pass to the second phase. The paper will be classified as 'uncertain' when the information in the title/abstract cannot answer the questions. However, when both reviewers are unclear, the article will pass to the following phase (VMS and WBD). Articles that present conflicts will be reviewed by the third reviewer (SC) and discussed amongst all three (VMS, WBD and SC).

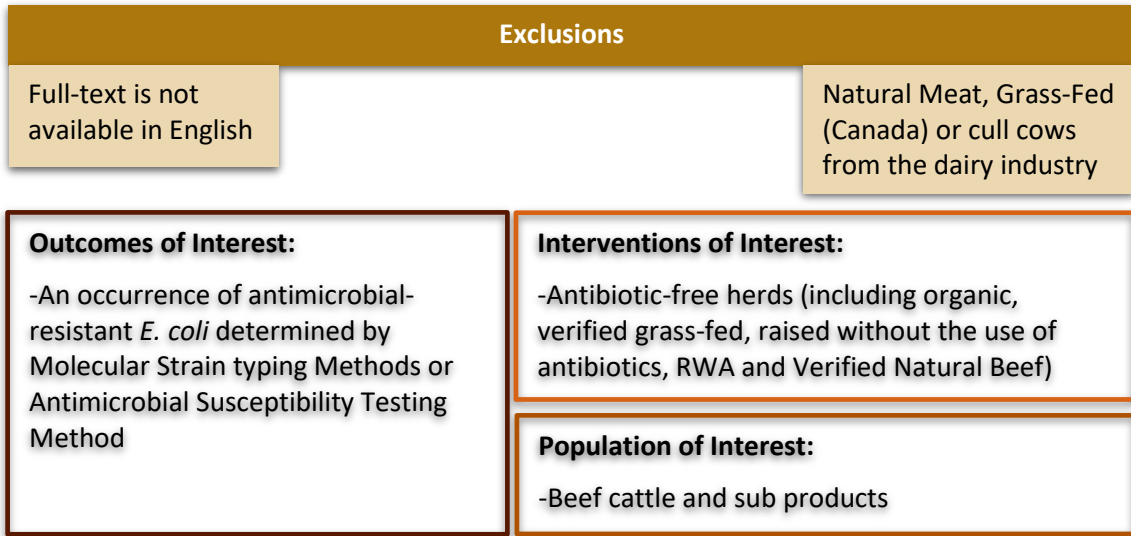
Second phase

The full-text screening will be done, emphasizing the methodology and results section.

- Is the article relevant to beef cattle?
- Does the article refer to faecal and/or environmental and/or meat samples?

Articles receiving a combination of 'yes' or 'uncertain' will be included, while those receiving a 'no' will be rejected.

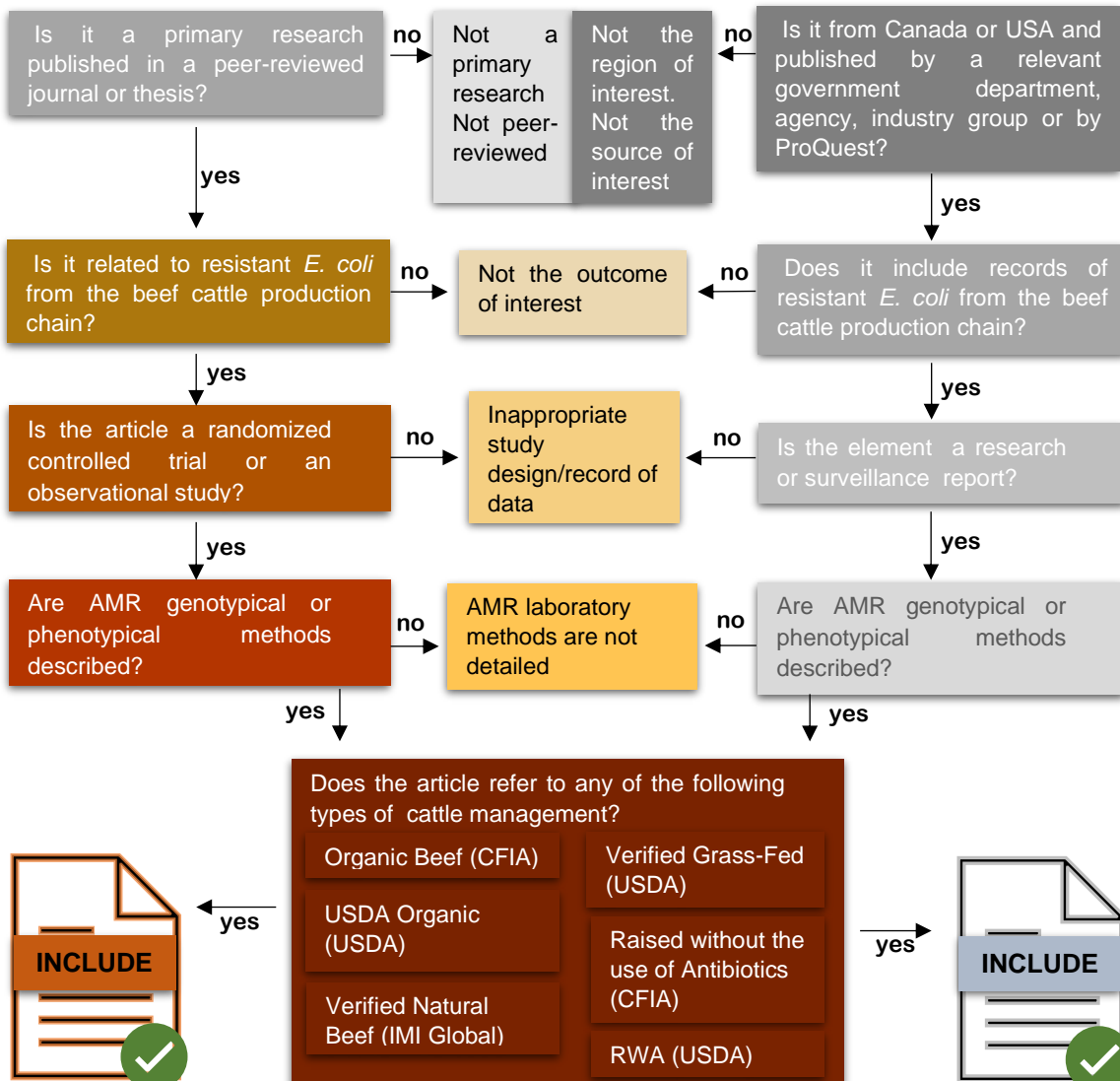
Screening Criteria for 'Exploring Antimicrobial Resistance in Escherichia coli: A Scoping Review Protocol Comparing Antibiotic-free and Conventionally Raised Beef Cattle in North America.'



Screening Questions

Reasons for Exclusion

Grey Literature



Grey literature

The Grey literature will undergo three instances: identifying the source, screening, and inclusion.

Eligibility criteria for grey literature

Inclusion criteria

- They were published by a government department, agency, industry group, or ProQuest Dissertations within Canada or the United States of America.
- Available in English
- The most current version of the document
- Research or surveillance reports
- Related to the entire beef production continuum
- Includes the records of at least one of the following groups
 - **Outcome of interest:** Resistant *Escherichia coli* (and search alternatives)
 - **Samples:** Faecal, meat (abattoirs, slaughterhouses, retail), environmental (soil, manure, air, water, facilities)
 - **Production Unit:** Organic beef (CFIA), USDA Organic (USDA), Verified Grass-Fed (USDA), Raised Without the Use of Antibiotics (CFIA), RWA (NSF), and Verified Natural Beef (IMI Global).

Exclusion criteria

- Natural meat (Canada)
- Grass-fed (Canada)
- Cull cows from the dairy industry

Information sources of grey literature

Grey literature database

Database of relevant government departments and agencies' publications:

- Canada Commons

Database of Dissertations:

- ProQuest LLC

Targeted websites

Websites of the beef cattle industry and/or surveillance programs

1. Canadian Food Inspection Agency
2. Public health agency of Canada
 - Centre for Food-borne, Environmental and Zoonotic Infectious Diseases

(CFEZID)

- Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS)
- National Enteric Surveillance Program (NESP)
- FoodNet Canada
- National Studies on Acute Gastrointestinal Illness (NSAGI)

3. United States Department of Agriculture (USDA)

- Economic Research Service (ERS)
- National Institute of Food and Agriculture (NIFA)

4. Centers for Disease Control and Prevention (CDC)

- National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS)
- PulseNet USA
- National Action Plan for Combating Antibiotic-Resistant bacteria (CARB)

5. The Livestock Conservancy

Websites of organic farming and similar certifications

- Organic Alberta
- Canada Organic Trade Association
- Safe Food for Canadians Regulations (SFCR)
- Canadian Food Inspection Agency – Raised Without the Use of Antibiotics

- National Sanitation Foundation (NSF International)-Raised without Antibiotics (RWA)
- American Grassfed Association (AGA)

Search strategy for grey literature

The search strategy will include the same groups of terms (with alternatives) previously stated for the peer-reviewed articles: (a) resistant *Escherichia coli*, (b) organic, and (c) beef cattle. A librarian (HG) will conduct the grey literature search and import eligible results in PDF format into Covidence. These will be assigned as ‘records identified from other sources.’

Studies will undergo two phases in the screening: Two independent reviewers will conduct data in both screening phases (VMS, WBD). Disagreements will be resolved by another independent reviewer (SC).

The first phase will be focused on the title and abstract. However, since abstracts are usually absent in these elements, the abstract, executive summary or table of contents (whichever is provided) will be examined [12].

- Is there a full text available in English?
- Does the title or abstract/executive summary/table of content suggest resistant *E. coli* from antibiotic-free or antibiotic-free and conventional beef cattle production chains?

The second phase will be focused on full-text screening.

- Is the element relevant to beef cattle?
- Does the element refer to faecal and/or environmental and/or meat samples?

Data extraction

Data obtained will be extracted using Covidence Extraction tool 2.0 and exported into Microsoft Excel 365 by two independent reviewers (VMS and WBD), while the third reviewer will solve conflicts (SC) and oversee the extraction process.

The data to be extracted will include:

- **General information:** Title, country, year, authors, funding.
- **Study design:** RCT or observational study, sample type, sample and size calculation.
- **Population characteristics:** Production system, type of management, breed, age, sex.
- **AMR technique to assess:** Specify which antimicrobial molecular/susceptibility technique was used, as determined by Molecular Strain typing Methods (whole-genome sequencing, MLST, WGS, PFGE, PCR, other molecular biology, or epidemiological methods) or Antimicrobial Susceptibility Testing Method (disk diffusion, microbroth dilution, Estrip), selective media.
- **Outcomes:** Prevalence of antimicrobial-resistant *E. coli*. Type of Antimicrobial Resistance Molecular detection throughout phenotypical and/or genotypical methods, statistical significance.

Data synthesis

A narrative review will be constructed based on the data collected. A meta-analysis will be executed if the data is homogeneous and sufficient.

CONCLUSIONS

The main reason to lead this scoping review is to meticulously examine research in the area of antimicrobial-resistant *E. coli* of antibiotic-free and conventionally raised beef cattle from North America. This scoping review will identify gaps in knowledge that require research in the future.

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APPENDIX A

CAB Abstracts search strategy

This strategy will be translated to syntax and vocabulary of the other databases mentioned in the Methods.

CAB Abstracts search (Ebsco platform, no date restrictions)

Date run: April 24, 2023

Search #	Search string	Results
S1	DE "beef cattle" OR DE "beef herds" OR DE "suckler herds" OR DE feedlots OR DE "meat and livestock industry" OR DE supermarkets	39,950
S2	TI (beef OR suckler* OR cattle OR cow* OR heifer* OR steer* OR stocker* OR bull* OR "cow-calf" OR feedlot* OR meat OR carcass* OR abattoir* OR slaughterhouse* OR retail OR supermarket* OR butcher*) OR AB (beef OR suckler* OR cattle OR cow* OR heifer* OR steer* OR stocker* OR bull* OR "cow-calf" OR feedlot* OR meat OR carcass* OR abattoir* OR slaughterhouse* OR retail OR supermarket* OR butcher*)	730,469
S3	S1 OR S2	732,719
S4	DE "Escherichia coli" OR DE "Escherichia coli infections"	121,062
S5	TI ("Escherichia coli" OR "E. coli" OR coliform* OR enterobacteriaceae OR enterobacteria* OR enteropathogen*) OR AB ("Escherichia coli" OR "E. coli" OR coliform* OR enterobacteriaceae OR enterobacteria* OR enteropathogen*)	164,974
S6	(DE "drug resistance" OR DE "multiple drug resistance") AND (DE "antiinfective agents" OR DE "antibacterial agents" OR DE "antibiotics")	51,423
S7	TI (resistan* OR toleran*) OR AB (resistan* OR toleran*)	839,896
S8	S4 OR S5 OR S6 OR S7	986,644
S9	DE "organic farming"	25,741
S10	TI (Organic OR certified OR "raised without" OR (free N3 antibiotic*) OR RWA OR "sustainable beef" OR "National Farm Animal Care Council" OR "grass fed" OR "pastured fed" OR "verified natural") OR AB (Organic OR certified OR "raised without" OR (free N3 antibiotic*) OR RWA OR "sustainable beef" OR "National Farm Animal Care Council" OR "grass fed" OR "pastured fed" OR "verified natural")	452,327
S11	S9 OR S10	454,220
S12	S3 AND S8 AND S11	1,609