

The prevalence of *Campylobacter* in live chicken, swine, turkey, and cattle on farms run under commercial conditions in the United States and Canada: a protocol for a systematic review and meta-analysis

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Author contributions:

MP will serve as review leader, and therefore will be responsible for performing primary and secondary screening, data extraction, risk of bias assessment, and the meta-analysis. MP is responsible for preparing all drafts of the protocol and the final manuscript, with input from all authors. MP developed the search strategy, risk of bias assessment strategy and data extraction criteria with input from JS. All authors read, provided feedback and approved the protocol.

Registration:

This protocol is archived in the University of Guelph's repository (The Atrium: <https://atrium.lib.uoguelph.ca/xmlui/handle/10214/10046>) and published online with Systematic Reviews for Animals and Food (SYREAF) available at: <http://www.syreaf.org/>. The systematic review will be reported using the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement guidelines (Liberati et al, 2009). This protocol uses the headings recommended in the PRISMA-P guidelines (Moher et al, 2015).

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Introduction.

Rationale:

In Canada and the U.S., approximately 38.0 and 14.3 out of every 100, 000 people, respectively, become ill from *Campylobacter* every year (Kaakoush, 2015). *Campylobacter* is also one of the main causes of gastroenteritis globally (WHO, 2018). Although usually mild, *Campylobacter* infections can cause severe illness and death in young children and immunocompromised people (WHO, 2018). The main route of transmission is foodborne, via undercooked meat products and unpasteurized dairy products (WHO, 2018). It is carried in the intestinal tracts of animals, and transmission between livestock on farms is usually via the fecal-oral route. Water and fomites can also be routes of transmission on farms. In addition, carcasses can be contaminated via feces at slaughter, transmitting the disease to humans through contaminated animal products (WHO, 2018). *Campylobacter* in poultry is the most frequently reported source of infection in humans (Bae et al, 2005). Although it causes illness in humans, it rarely causes illness in animals, which can make on farm detection difficult (WHO, 2018). Due to the burden of disease in humans, and

the potential consequences, quantifying the burden of *Campylobacter* in livestock populations is essential in efforts directed at reducing the risk of foodborne illnesses.

Campylobacter in livestock has been reported globally. However, studies tend to focus on one or two livestock species, and a synthesis of the prevalence across livestock species in the U.S. and Canada is lacking. Although animals can be contaminated during slaughter, at retail, and on farm, it is useful to examine the prevalence of *Campylobacter* in live animals on farm, since information regarding prevalence in live animals is the start of the farm-to-fork production chain and will be the most useful in reducing risk further down the production chain. By determining the relative frequency of *Campylobacter* in different species, efforts can be made to understand the point of contamination on farm and to take the appropriate measures to address contamination and reduce prevalence. A systematic review and meta-analysis of the prevalence of *Campylobacter* on livestock farms operated under commercial conditions in the U.S. and Canada will be undertaken. This will produce the highest level of evidence for establishing the overall prevalence of *Campylobacter* within livestock in the two countries. The review can provide baseline data for targeting additional research to control the presence of *Campylobacter* on farms.

Objectives: The objective of this protocol is to describe the methods of designing a systematic review to address the question: “What is the prevalence of *Campylobacter* (*coli*, *jejuni*, or *spp.*) in live chicken, cattle, turkey and swine in the United States and Canada?”

The specific PO items, which define the eligibility criteria, are as follows:

- i. *Population:* Live chicken, cattle, turkey, and swine on farms run under commercial conditions in the United States and Canada. Live chicken farmed for meat will be included only, since eggs are not usually contaminated with *Campylobacter* (Seafood, n.d.).
- ii. *Outcome:* The outcome of interest is the prevalence of *Campylobacter* (*coli*, *jejuni*, or *spp.*) during any period of time.

Methods

Eligibility criteria: In addition to the eligibility criteria above, publications will be limited to those published in English and in French. Samples must be either fecal or cecal.

Exclusion criteria: Non-primary research studies, studies with a deliberate disease induction (e.g., challenge studies) and studies that only report resistant strains of *Campylobacter* will be excluded from this systematic review.

Study designs eligible: Observational study designs, with the exception of case-control studies.

Information sources:

Table 1: Databases and information sources to be searched

Database / information source	Interface / URL
MEDLINE	PubMed
CAB Abstracts	CAB Interface
Science citation index	Web of Science
Agricola	Proquest
Government publications (grey literature)	FoodNet Canada annual reports; USDA APHIS website

Search strategy:

A Science Citation Index (Web of Science) search strategy designed to identify studies of the prevalence of *Campylobacter* in live animals on farms in the U.S. and Canada is presented in Appendix 1. The search strategy employs a multi-stranded approach to maximize sensitivity using key words associated with the following concepts:

- Livestock;
- AND
- Prevalence;
- AND
- Location;
- AND
- *Campylobacter*

The searches will be limited by language and will not be limited by date. The specific search strategies will be created with input from a librarian with experience in systematic review searching. Searches will be conducted using each database listed in the protocol. With the help of a librarian, each search strategy will be translated to appropriately reflect the differences in the interfaces and functionality of each database. The proposed science citation index strategy is included in Appendix 1, with the results from a preliminary search.

Study records:

Data management:

Selection process: Abstracts and titles will be screened for eligibility by two reviewers. The following questions will be used to determined relevance:

- 1) Does the title and abstract describe a primary study reporting the prevalence of *Campylobacter (jejuni, coli, or spp.)*?
YES (neutral response), NO (exclude), UNCLEAR (neutral response)

2) Eligible population: Does the study include live chicken farmed for meat, swine, cattle, or turkey at any stage of production?

YES (neutral response), NO (exclude), UNCLEAR (neutral response)

3) Is the primary study an observational study?

YES (neutral response), NO (exclude), UNCLEAR (neutral response)

4) Is the full text available in English or French?

YES (include for full text screening), NO (exclude), UNCLEAR (neutral response)

If both reviewers respond “no” to a question, then that article will not move on to the full text screening stage. Any disagreement will be resolved by consensus or by arbitration with a third reviewer. Articles where all questions are answered “yes” or “unclear” will move on to full text screening.

Following the title/abstract screening, full texts for potentially relevant articles will be obtained using University of Guelph resources. The full-text of these articles will be screened for eligibility using the questions below. Two reviewers will review each full-text article, and any disagreement will be resolved by consensus or, if consensus cannot be reached, by arbitration with a third reviewer.

1) Is the full-text available > 500 words?

YES (neutral response), NO (exclude)

2) Is the full-text available in English or French?

YES (neutral response), NO (exclude)

3) Is the study based out of the United States or Canada, OR are all of the authors affiliated with one or both of the countries?

YES (neutral response), NO (excluded)

4) Is the primary study an observational study?

YES (neutral response), NO (exclude)

5) Does the primary study report the prevalence of *Campylobacter (jejuni, coli, or spp.)*?

YES (neutral response), NO (exclude)

6) Eligible population: Does the study include live chicken farmed for meat, swine, cattle, or turkey at any stage of production?

YES (neutral response), NO (exclude)

7) Eligible outcome: Is the prevalence of *Campylobacter jejuni, coli, or spp.* reported? Studies that only report the prevalence of resistant *Campylobacter spp.* are to be excluded.

YES (neutral response), NO (exclude)

8) Are the target species on commercial farms or raised under commercial conditions?

YES (neutral response), NO (exclude)

Data collection process: Data will be extracted by two independent reviewers, and any disagreements will be resolved by consensus or a third reviewer. Authors will not be contacted to retrieve missing data or to receive clarification. A form for data extraction will be created in Distiller SR®.

Data items:

Study level data to be extracted include:

- 1) Authors
- 2) Year of publication
- 3) Location where the study was conducted (province/state, country) or country of the affiliated authors if the location is not specified.
- 4) Year(s), month(s) or season(s) the study was conducted

Farm level data collected:

- 1) Livestock species
- 2) Source of samples (fecal or cecal)
- 3) Laboratory method used to identify *Campylobacter* (culture or DNA)
- 4) Age or stage of production of the livestock

Outcomes:

- 1) Prevalence of *Campylobacter*
- 2) Species of *Campylobacter*
 - a. *Coli, jejuni*, or unspecified
 - b. Laboratory method used to identify the species (culture or DNA)

Outcome data to be collected separately for each species of animal and each species of Campylobacter:

- 1) Prevalence
 - a. Level at which the outcome data were measured (farm level, individual level, or pooled)
 - i. Farm level: Number of samples needed to define positive farm, number of samples collected per farm, number of positive farms, number of farms sampled
 - ii. Individual level: Number of positive samples, total number of samples, and number of farms
 - iii. Pooled: Number of samples per pool, number of positive pools, total number of pools, and number of farms
- 2) Variation

Outcomes and prioritization

The primary outcome is the prevalence of *Campylobacter spp.* in live chicken, swine, turkey, and cattle on farms run under commercial conditions in the United States and Canada. Prevalence estimates will be prioritized over raw data (i.e., number with *Campylobacter* and total number sampled). Raw data will be extracted if prevalence estimates are absent.

Risk of bias in individual studies:

A version of the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool that has been modified for prevalence studies will be used (Broen, 2012). The tool will further be modified to address this particular review. The criteria for assessing bias using the modified QUADAS-2 tool has been outlined in Appendix 2.

Data synthesis

To summarize the findings, we will conduct a meta-analysis using R Studio. A meta-analysis will be conducted for each livestock species (e.g., prevalence of *Campylobacter* in chicken, prevalence of *Campylobacter* in swine) and species of *Campylobacter* using a random effects approach given the *a priori* assumption of heterogeneity. Subgroup meta-analysis will be done on pooled vs individual samples vs farm level prevalence. Estimates from individual studies will be transformed using the Freeman-Tukey arcsine transformation to stabilize the variance.

Heterogeneity will be assessed using Cochrane's Q test and I^2 . Laboratory method (e.g., culture or DNA), production stage, sampling source (e.g., cecal or fecal), and whether the main objective of the study is to estimate prevalence are all potential sources of heterogeneity and will be examined if there are at least two studies per category. Potential sources of heterogeneity will be addressed with a meta-regression.

Discussion:

This systematic review and meta-analysis will provide a synthesis of the current prevalence of *Campylobacter spp.* in various livestock species on farms run under commercial conditions in the United States and Canada. Results will be helpful in directing future intervention studies to reduce the prevalence of *Campylobacter spp.* on farms and improve food safety.

References:

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Appendix

Appendix 1:

A preliminary search was conducted in the science citation index (Web of Science platform) on 03/May/2019

- a) Livestock [search lines 1-4]
- b) Prevalence [search line 5]
- c) Location [search line 6]
- d) *Campylobacter* [search line 7]

#	Searches	Results
1	TS= (cow* OR cattle OR calve* OR dairy OR beef OR bovine)	591,791
2	TS= (chicken* OR poult* OR fowl OR cock* OR chick* OR hen* OR broiler* OR fryer* OR “gallus gallus domesticus”)	2,579,380
3	TS= (turkey*)	120,003
4	TS= (swine OR porcine* OR sow* OR pig* OR hog* OR boar* OR “Sus scrofa”)	895,176
5	TS= (prevalence OR proportion* OR percentage* OR frequency OR portion* OR magnitude* OR fraction* OR distribution*)	7,481,235
6	TS= (Canad* OR United States OR North America OR U.S. OR U. S. OR U.S.A. OR US OR American* OR America OR states OR province* OR Ontario OR Quebec OR Nova Scotia OR Alberta OR Saskatchewan OR Manitoba OR Prince Edward Island OR P.E.I OR New Brunswick OR British Columbia OR B.C OR Washington OR Montana OR North Dakota OR Minnesota OR Wisconsin OR Michigan OR Ohio OR Pennsylvania OR New York OR Vermont OR Maine OR New Hampshire OR Massachusetts OR Rhode Island OR Connecticut OR New Jersey OR Delaware OR Maryland OR Washington D.C. OR West Virginia OR Virginia OR Indiana OR Illinois OR Iowa OR South Dakota OR Nebraska OR Wyoming OR Idaho OR Oregon OR Nevada OR California OR Arizona OR Utah OR Colorado OR Kansas OR Oklahoma OR Arkansas OR Missouri OR Tennessee OR Georgia OR Florida OR Alabama OR Alaska OR North Carolina OR Kentucky OR New Mexico OR Texas OR Louisiana OR Mississippi OR South Carolina)	7,506,646
7	TS= (Campylobacter OR Campylobacteriosis OR Campylobacter jejuni OR “Campylobacter coli” OR c.coli OR c.jejuni)	25,304
8	#1 AND #5 AND #6 AND #7	269
9	#2 AND #5 AND #6 AND #7	482
10	#3 AND #5 AND #6 AND #7	76
11	#4 AND #5 AND #6 AND #7	149

Appendix 2:

Modified version of the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool: criteria for prevalence studies.

Criteria #	Question
1	The final sample should be representative of the target population. At least 1 of the following should apply for the study: <ol style="list-style-type: none">1. An entire target population2. Randomly selected sample3. Sample shown to represent the target population
2	Was the objective of the study to measure the prevalence of <i>Campylobacter</i> or was this a by-product of another study design?
3	Was the study adequately powered to detect a prevalence of 10% (or 90%) with a 5% allowable error?