

A Protocol for a Scoping Review to Examine Studies Investigating Zoonotic Diseases in *Canis familiaris* in North America Since the Beginning of the 21<sup>st</sup> Century.

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**Introduction****Rationale**

While animals, including dogs, provide many health benefits to humans<sup>1,2</sup>, dogs can harbour zoonotic diseases that can be directly transmitted to humans, resulting in a range of infection from subclinical to serious and potentially life-threatening disease<sup>3-6</sup>.

Canine zoonotic diseases are present in many countries across the world but their endemicity varies on the basis of certain socio-economic influences including, but not limited to: availability of animal and human health resources, income, and the predominance of closely shared living environments<sup>8</sup>. While dog-related zoonotic diseases represent a major public health concern irrespective of country-status<sup>9-12</sup>, the nature and level of that concern may vary, depending on local socio-economic influences.

North America comprises 16.5% of the earth's land mass<sup>13</sup>. The Inequality-adjusted Human Development Index (IHDI), developed by the United Nations Development Programme (UNDP), describes the average achievements of a country on the basis of health, education and income, while taking into account the human development cost of inequality<sup>7</sup>. North American comprises sovereign states and dependent territories classified as "very high", "high", "medium" and "low" human development according to the IHDI<sup>7</sup>. and within which previous studies have identified canine zoonoses<sup>14-17</sup>.

While opportunities for the transmission of zoonoses from animals to humans has been described as a complex global problem driven largely by a series of socio-economic factors (*i.e.* biological, ecological, political and socio-economic), it is also significantly influenced by if, how, where and when people interact with animals<sup>18,19</sup>. The inclusion of integrated collaborative approaches

to health research (*i.e.* One Health, EcoHealth) thus provides a mechanism to address complex global health problems including those posed by canine zoonoses, while increasing the ability to identify sustainable health solutions.<sup>20,21</sup>

A synthesis of research on canine zoonoses taking into account a standardized indicator of socio-economic factors across countries, such as the IHDI, could enhance knowledge and understanding of the health of domestic dogs within a given period and concomitantly, the potential ways in which dogs may be contributing to human disease in this part of the world.

This protocol describes the methods for conducting a scoping review, which will describe the extent, methodologies, and general characteristics of the literature, including proposed integrated collaborative approaches to health in studies investigating canine zoonoses in domestic dogs in North America.

This review will follow the framework developed by Arksey and O'Malley<sup>22</sup> and further enhanced by the Joanna Briggs Institute methodology guidance for scoping reviews<sup>23</sup>.

## **Research Question and Objectives**

The broad research question guiding the review is: *‘What is known about canine zoonoses in domestic dogs from the existing literature in the continent of North America, and how does the literature on canine zoonoses vary across the continent?’*

The goal of this review will be to: Identify, characterize, and map the available literature in comparison to state/territory ranking on the current Inequality-adjusted Human Development Index (IHDI), in order to:

1. Identify the studies related to types of canine zoonoses in domestic dogs that have been published in North America since the beginning of the 21<sup>st</sup> century
2. Identify the main objectives and types of study methodologies reported
3. Identify and characterize the research that has been conducted in “very high”, “high”, “medium” and “low” human development North American countries of North America; and,
4. Examine whether collaborative integrated approaches (*e.g.* One Health, EcoHealth and others) have been described by authors and how they report their inclusion.

## **Methods**

### ***Review Registration***

This protocol is archived in the University of Guelph’s institutional repository (The Atrium) and published online with Systematic Reviews for Animals and Food (SYREAF) available at: <http://www.syreaf.org/>

### ***Eligibility Criteria***

Studies will be eligible if they:

- Are original scientific reports of research findings (*i.e.* primary research studies) of animal-level and/or pathogen-level (*e.g.* studies relating to molecular epidemiology of pathogens that have been sampled from dogs) outcomes;
- Have been published in the English, French or Spanish languages;
- Have investigated any of the listed canine zoonoses or their disease-causing agent (**Table 1**) in the target population of interest
- Have been conducted in one or more North American countries and,
- Were published between January 1 2000 and the present.

Conference proceedings of less than 500 words and citations for which the full text document in English, French or Spanish is unavailable, will be excluded; all other primary research study designs relevant to answering the broad research question will be eligible.

### **Eligible Target Population of Interest**

Studies where the population of interest includes any breed of dog belonging to *Canis familiaris*, including owned and unowned domestic dogs, or the focus of interest is a disease-causing agent affecting dogs as a target population, will be eligible.

### **Eligible Diseases of Interest**

Studies investigating any of the canine zoonoses of known public health significance listed in **Table 1**, in the target population of interest will be eligible. The list of eligible diseases was developed on the basis of their relevance to dogs and humans: For the purposes of the scoping review for which this protocol has been developed, relevant canine zoonoses are defined as diseases of domestic dogs which have potentially serious (morbidity and/or mortality) dog and human health and economic impacts within the countries/regions of interest.

Relevant canine zoonoses terms (**Table 1**) were accessed from a combination of published literature and books as well as relevant region-specific organizations including the: Pan American Health Organization (PAHO); Canadian Food Inspection Agency (CFIA); World Health Organization (WHO); World Organisation for Animal Health (OIE); Centre for Food-borne, Environmental and Zoonotic Infections (via the Public Health Agency of Canada (PHAC)); and, US Centers for Disease Control and Prevention (CDC)).

### **Eligible Countries (including within-country regions) of Interest**

Any country (or region within) listed as part of North America<sup>13</sup> including: Anguilla; Antigua and Barbuda; Aruba; The Bahamas; Barbados; Belize; Bermuda; Bonaire; British Virgin Islands; Canada; Cayman Islands; Clipperton Island; Costa Rica; Cuba; Curacao; Dominica; Dominican Republic; El Salvador; Federal Dependencies of Venezuela; Greenland; Grenada; Guadeloupe; Guatemala; Haiti; Honduras; Jamaica; Martinique; Mexico; Montserrat; Navassa Island; Nicaragua; Nueva Esparta; Panama; Puerto Rico; Saba; San Andres and Providencia; Saint Barthelemy; Saint Kitts and Nevis; Saint Lucia; Saint-Martin; Saint Pierre and Miquelon; Saint Vincent and the Grenadines;; Sint Eustatius; Sint Maarten; Trinidad and Tobago; Turks and Caicos Islands; United States; and the United States Virgin Islands.

## ***Identifying Relevant Studies***

An initial broad search of the literature of one electronic database was conducted by DAJ in April 2018. A list of the search terms is shown in Appendix I, **Table 1**. Comprehensive literature searches will be conducted through the McLaughlin Library, University of Guelph in the following electronic databases: AGRICOLA<sup>®</sup>, CAB Direct<sup>®</sup>, PubMed<sup>®</sup> via NCBI<sup>®</sup>, and, the Science Citation Index Expanded (SCI-EXPANDED)<sup>™</sup>, and Emerging Sources Citation Index (ESCI)<sup>™</sup> databases via the Web of Science platform<sup>™</sup>, **Table 2**.

Key word searches were developed from the findings of the initial broad search and will include combinations of variations of the concept terms “dog” and applicable canine zoonoses with the controlled vocabulary option included where available. The search strategy will be modified for each database accounting for differences in syntax, indexing, and functionality where appropriate.

The literature search will be conducted in May 2018 and limited to English, French or Spanish language studies published between 2000 and 2017.

## ***Data Management***

Search results will be uploaded into Mendeley<sup>®</sup> reference management software and duplicates removed. Information relating to the number of studies found, duplicates removed, and the final studies included in the scoping review will be presented in the final report using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)<sup>®</sup> flowchart template.

## ***Study Selection***

**Level 1** and **Level 2** screening for eligibility will be completed by DAJ and other reviewers, working independently. To enhance rigor and reliability between reviewers, training exercises will be conducted and interrater reliability scored between the two reviewers prior to commencing screening.

**Level 1:** Title, abstract, and index terms will be screened for relevance using the following questions, with the response options “yes”, “no”, and “unclear”. Keywords pertaining to the question will be listed where relevant for clarity:

1. Does the title/abstract describe primary research?
2. Does the title/abstract investigate canine zoonoses in the primary target population (i.e. dogs)?
3. Was the study conducted in North America?

Studies will be excluded if both reviewers agree that the answer is “no” to any of the above questions.

**Level 2:** Screening will be conducted on full text publications for studies that meet the “yes” answer or “unclear” answer to Level 1 screening questions.

The following questions will be used for Level 2 eligibility screening and data extraction with answers “yes” or “no” only. Studies will be excluded if both reviewers are in agreement in answering “no” to any of the following questions:

1. Is the full text publication a journal article or conference proceeding (>500 words)?
2. Is the full text article or conference proceeding (>500 words) describing a primary research study?
3. Is the full text article available in English, French or Spanish?
4. Has the primary research been published or presented (*e.g.* conference proceedings (> 500 words)) within the period 2000 – present?
5. Does the full text research investigate one or more canine zoonoses of interest?
6. Has the full text research been conducted in North America?
7. Is the study at the dog-level or pathogen-level where the zoonotic pathogen was isolated from a dog?
8. In the full text publication, are domestic dogs the target population?

Discrepancies on eligibility between the two reviewers at both levels will be resolved by consensus and mediated by another co-author if consensus cannot be reached. Please note that Level 2 eligibility screening and data extraction on non-English articles will be completed by a single reviewer (CF).

### ***Data Extraction Strategy***

Full text publications will be acquired and uploaded into the commercial review management program DistillerSR™ (Evidence Partners, Ottawa, Canada).

Data extraction will be completed using structured pre-tested forms created in DistillerSR™ that will include:

**General study characteristics:** Publication year; North American country(ies) in which the study was conducted; and, whether any type of integrated collaborative approach (as described in the protocol rationale) was listed included in the study (*e.g.* in the objectives or methods).

**Study population:** Domestic dogs (owned or unowned); and sample size(s).

**Disease(s) investigated:** The canine zoonosis(es) investigated in domestic dogs.

**Focus of study:** Dog-level or pathogen-level.

**Study approach (answer these questions if focus of study is dog-level):** Pre-identified categories of why the study was conducted including:

- **Descriptive:**
  - Outbreak investigation

- Case-reports (study describes rare condition or an unusual manifestation of a more common [canine zoonotic] disease(s) in dogs),
- Case-series reports (study describes occurrence of or usual clinical presentation of canine zoonotic condition/ disease) and,
- Descriptive surveys (study estimates frequency and distribution of selected outcomes (*i.e.* canine zoonoses) in defined canine population)).
- **Analytical:**
  - Experimental hypothesis-testing
    - Challenge trial of intervention to prevent (*i.e.* when an experiment is conducted in domestic dogs with a deliberate disease induction (e.g. vaccination then exposure to an infectious disease agent)).
    - Challenge trial of intervention to treat (*i.e.* when an experiment is conducted in domestic dogs with a deliberate disease induction (e.g. exposure to an infectious disease agent and after onset of clinical signs, then treatment)).
    - Natural disease trial of intervention to prevent (*i.e.* controlled trial, field trial or clinical trial).
    - Natural disease trail of intervention to treat (*i.e.* controlled trial, field trial or clinical trial).
  - Observational study hypothesis-testing
    - Intervention to prevent
    - Intervention to treat
    - Evaluation of risk factors for disease
    - Evaluation of mechanisms of disease / virulence
    - Diagnostic test development / evaluation

### **Study approach if Pathogen-Level Studies:**

Data will be collected on the premise for conducting the pathogen-level studies including whether the study, specific to the pathogen, was focused on: Molecular biology (for instance phage typing or serotyping of bacteria, describing surface proteins or antigens of viruses, characterization of nucleic acids (DNA; RNA)); phylogeny (molecular epidemiology); whole genome sequencing; identification of virulence factors; development or validation of laboratory methods and diagnostics; pathophysiology and immunology of pathogen-host interaction (e.g., evaluating interleukin).

Following data extraction process, the Inequality-adjusted Human Development Index (IHDI) will be derived based on the country of publication.

### **Results Strategy**

#### ***Charting the Data***

Study analysis will include descriptive analysis of study characteristics, target population and study approach.

### ***Collating, Summarizing and Reporting the Results***

A combination of figures and tables will be used to collate, summarize and report study results. A figure will be used to depict the scoping review flow chart detailing the process of study inclusion. Tables will be used to collate, summarize and report the primary level of study categorization prioritized by publication type (*i.e.* Descriptive - Case reports, Case series, Descriptive surveys; Analytical experimental; Analytical observational; Conference proceedings; Study approach unclear).

Secondly, descriptive and analytical studies will be further categorized by: Year of publication; country of origin within the region of interest; resource setting; integrated collaborative approach(es) proposed; target population (owned/unowned domestic dogs); and canine zoonoses investigated.

### **Discussion**

This scoping review will provide a synthesis of primary research investigating canine zoonoses in domestic dogs that has been conducted in North America during 2000 - 2017. Results can be used to inform future scientific research studies inclusive of systematic reviews, government policy and public health strategies relating to canine zoonoses in multiple countries in this part of the world.

### **Competing interests**

The authors have no competing interests to declare.

### **Authors' contributions**

DAJ will serve as corresponding author and PhD student leader on the scoping review, and will be responsible for coordinating the scoping review, training the second reviewers, performing primary and secondary screening, data extraction analyzing, summarizing and reporting the results. DAJ is responsible for preparing all drafts of the protocol and the final manuscript, with input on content from JMS, CF, and SLH. Search strategies will be developed and performed by DAJ with input from AMV. JMS will act as methodological expert and will participate as a reviewer. Additionally, CF will act as a reviewer for French and Spanish language studies. The second reviewer will perform primary and secondary screening, participate in data extraction and in the analysis of results. All authors will contribute to, and approve, the final manuscript.

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**Appendix I:** Initial search strategy and selected electronic databases

**Table 1** Initial broad search of the literature of one electronic database

<b>Database:</b>	<b>PubMed via NCBI</b>
<b>Search period:</b>	2000 – 2018
<b>Library:</b>	McLaughlin Library, University of Guelph
<b>Date of Search:</b>	Monday May 14, 2018
<b>Limits:</b>	Advanced Search Builder in Title/Abstract <b>Filters activated</b> Publication date (custom date range) 2000-01-01 to 2018-12-31; Species: Other Animals; Languages: English, French, Spanish; Text availability: Abstract
<b>Search terms:</b>	Domestic dog descriptor terms: “domestic dog” OR “Canis familiaris” OR canine OR chien OR perro AND Canine Zoonotic Diseases descriptor terms: Anaplasma OR Ancylostoma OR Babesia OR Bacillus OR “Baylisascaris procyonis” OR “Borrelia burgdorferi” OR Brucella OR “canine zoono*” OR Campylobacter OR Capnocytophaga OR Corynebacterium OR “Coxiella burnetii” OR “Cryptosporidium parvum” OR “Dipylidium caninum” OR “Echinococcus granulosus” OR “Echinococcus multilocularis” OR Ehrlichia OR “Entamoeba histolytica” OR “Escherichia coli” OR “Giardia intestinalis” OR Helicobacter OR Influenza OR “Leishmania chagasi” OR “Leishmania infantum” OR Leptospira OR “Methicillin resistance staphylococcus aureus” OR “Microsporum canis” OR “Onchocerca lupi” OR Pasteurella OR Pseudomonas OR Proteus OR Rabies OR “Rickettsia rickettsii” OR Salmonella OR “Sarcoptes scabiei” OR Spirocerca OR “Sporothrix schenckii” OR “Toxocara canis” OR “Toxoplasma gondii” OR “Trichinella spiralis” OR “Trypanosoma cruzi” OR “Uncinaria stenocephala” OR “Vibrio cholerae” OR “Yersinia enterocolitica”
<b>Number of articles:</b>	3,628

**Table 2** Platforms and the electronic databases within which keyword searches will be conducted of canine zoonoses in domestic dogs in North America.

<b>Database</b>	<b>Platform:</b>
PubMed	NCBI©
CAB Direct	CABI©
AGRICOLA	ProQuest®
SCI-EXPANDED	Web of Science™
ESCI	Web of Science™