Antimicrobial Resistant *Campylobacter* species in the Food Chain: Understanding the Human Risk of Infection

by

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THESIS ABSTRACT

Background: *Campylobacter* spp., commonly detected in poultry, are the third most common cause of foodborne illness in Canada. *Campylobacter* while self-limiting and typically only requiring supportive care treatment, can be resistant to antimicrobials important to human health. To better understand the dissemination of antimicrobial resistant *Campylobacter,* the overall objective of this thesis was to investigate the human exposure to, and risk from, antimicrobial resistant *Campylobacter* in Canada. In addition to investigating transmission pathways in general, because of the contribution of chicken meat to *Campylobacter* spread, this thesis also investigated the potential exposure from broiler chickens.

Methods: A scoping review was used, following PRISMA guidelines and the Joanna Briggs Institute framework, to determine factors potentially associated with human infection with *Campylobacter* spp. that are resistant to fluoroquinolones, macrolides, or tetracyclines. An integrated assessment model component was developed to evaluate the probability of human exposure to antimicrobial resistant *Campylobacter* spp. from broiler chicken in Canada, specifically resistance to fluoroquinolones, tetracyclines, or macrolides, and identify knowledge and data gaps.

Results: The scoping review identified 8,527 de-duplicated articles and 27 articles were included after screening. Factors were broadly categorized into seven categories: animal contact, prior antimicrobial use, participant characteristics, food and food preparation, travel, underlying health conditions, and water. Articles exploring factors related to travel (n=17) and participant characteristics (n=14) were most common. The factors and regions studied, the types of investigations, and the knowledge they contributed were broad and diverse. The populations included, data sources utilized, and analyses employed varied greatly. Travel was an important

risk factor, and infections were commonly associated with gastrointestinal *Campylobacter jejuni* and were often evaluated using only a univariable analysis. Most of the studies were conducted in a small sample of high-income, westernized countries.

The integrated assessment model literature review identified 7,344 de-duplicated articles of which 15 articles were included in the qualitative synthesis after screening. Identified factors were allocated into the model at three stages of production: farm, abattoir, and retail. Factors included management practices, antimicrobial use on farm, chilling type at processing, and packaging type. Two scenarios were compared to a reference scenario to investigate:

1. How the Canadian context influenced human exposure to antimicrobial resistant *Campylobacter.*
2. How fluoro(quinolone) use in broiler chickens influenced human exposure to antimicrobial resistant *Campylobacter.*

Conclusions: This thesis contributed the first scoping review of potential factors associated with human infections with antimicrobial resistant *Campylobacter*. The heterogeneity of the results and articles provided a broad overview of the available factors while also illuminating areas for potential future research. These future research areas include studies examining time at risk and AMR, the effect of comorbidities that require antimicrobial use, and the recent effects of antimicrobial stewardship policies.

This thesis also represents the first integrated assessment model that brings together the body of literature to estimate human risk of exposure to antimicrobial resistant *Campylobacter* from broiler chicken in Canada. This model framework can now be used for future understanding of the risk of exposure of Canadians from the broiler production chain. The model also provided initial insights into factors that may influence the levels of antimicrobial resistant

Campylobacter in the broiler food chain while identifying substantial gaps in data and knowledge. The median estimated number of Canadians potentially exposed (NCPE) values ranged from 101.71 to 2,052.65 standardized per 100,000 and the maximum values ranged from 14.041.95 to 19,066.81 standardized per 100,000. One key result from the fluoroquinolone resistance model suggests that there is persistent fluoroquinolone resistant *Campylobacter* spp. in Canada in broiler chickens. Two important assumptions of interest were that modeled factors occurred independently of each other and that they also occurred concurrently. The model currently does not account for time or ordering of factors and did not have enough data to control and evaluate correlations or interactions between factors, which may affect external validity.

Lastly, this thesis suggests areas for future research including filling gaps in baseline surveillance data, a need for increased transparency about the prevalence of broiler chicken production types and extending the model past the retail node to include consumer practices and human health outcomes.

PREFACE

The work presented in this thesis is original work by Christine Neustaedter. Parts of this thesis have been previously presented at various conferences (below). No part of this work has been previously published in a peer-reviewed journal. A manuscript of chapter 2 was submitted for review to Epidemiology and Infection on May 7, 2022 (pending).

1. Neustaedter C, Reid-Smith RJ, MacKinnon MC, Carson CA, Murphy CP, Chapman B, Otto SJG. "What was in that food?!": A scoping review of risk factors for infection with antimicrobial-resistant *Campylobacter*. Poster presented at: This is Public Health Week; November 4-8, 2019; Edmonton, Canada.
2. Neustaedter C, Reid-Smith RJ, MacKinnon MC, Carson CA, Murphy CP, Chapman B, Otto SJG. "What was in that food?!": A scoping review of risk factors for infection with antimicrobial-resistant *Campylobacter*. Oral presentation at: Conference of Research Workers in Animal Diseases; December 4-8, 2020; virtual.
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DEDICATION

For Elizabeth “Betty” Schlichting

May 29, 1937 – August 14, 2020

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I would have given up long ago had it not been for Sammy Lowe, Dana Tschritter, and Misha Miazga-Rodriguez listening to my many rants and reassuring me of the light at the end of the tunnel. Thank you to my family for nudging me forward and for your support even though it meant moving two provinces over. Lastly, thank you to my friends in Manitoba and Alberta who remind me that there is life outside of school, for indulging in my procrastination, and for

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ABM	Agent-based modelling
AMR	Antimicrobial resistance
AMU	Antimicrobial use
ARG	Antimicrobial resistance gene
CARSS	Canadian Antimicrobial Resistance Surveillance System
CIPARS	Canadian Integrated Program for Antimicrobial Resistance Surveillance
CNISP	Canadian Nosocomial Infection Surveillance Program
FQL	Fluoroquinolone
GBS	Guillain-Barré Syndrome
iAM.AMR	Integrated Assessment Model for Antimicrobial Resistance
IBS	Irritable Bowel Syndrome
MCL	Macrolide
MFS	Miller Fisher Syndrome
NCPE	Number of Canadians potentially exposed
OR	Odds ratio
QL	Quinolone
QMRA	Quantitative microbial risk assessment
ReA	Reactive arthritis
TET	Tetracycline
WHO	World Health Organization

CHAPTER 1: INTRODUCTION AND BACKGROUND

1.1 Literature Review

1.1.1 Antimicrobial resistance

What is antimicrobial resistance and how does it develop?

Antimicrobial resistance is defined by the World Health Organization as the ability of a microorganism to stop an antimicrobial from working against it, rendering standard treatments ineffective (1). The organisms that can develop antimicrobial resistance include bacteria, viruses, parasites, fungi, and amoeba; while antimicrobials are classified as antibacterials, antivirals, antifungals, and antiparasitics (1). Antibacterials are further subdivided into classes, such as fluoroquinolones, macrolides, and tetracyclines and work to kill or inhibit the growth of bacteria in different ways (2). Antimicrobial resistance becomes an even greater issue when organisms develop resistance to multiple antimicrobials in different classes and sometimes to all drugs available for treatment. Organisms with multi-drug resistance are often defined as having resistance to at least one drug in three or more antimicrobial classes; extensively-drug resistant organisms are resistant to at least one drug in all but two or fewer antimicrobial classes; pan-drug resistant organisms are resistant to all available drugs in all antimicrobial classes (3). As more organisms become pan-drug resistant, we risk moving back into a pre-antibiotic era (1, 4).

Antimicrobial resistance can occur in different ways. Some organisms are intrinsically resistant to certain drugs either because the mechanism or target of the drug does not exist in that organism or the organism already naturally has the genes for physical characteristics needed to resist the antimicrobial (2). Organisms can also acquire resistance, either through genetic mutation or incorporating other genetic material in mobile genetic elements (MGEs) in the form of antimicrobial resistance genes (ARGs) through horizontal-gene transfer (2). Sometimes, genes

that carry resistance do so at a survival cost to the organism which may not flourish under normal circumstances (2). However, when these same organisms are in the presence of antimicrobials, the ARGs allow these organisms to survive and multiply, potentially replacing the wild-type susceptible organisms (5). Sometimes resistance adaptations are multi-purpose. For example, genes that increase the number of efflux pumps along the cell membrane can bring about resistance to fluoroquinolones but can also increase resistance to tetracyclines because these pumps remove both drug classes, referred to as cross-resistance (2). Co-selection, another important element to consider, occurs when ARGs are linked on a chromosome, plasmid or other MGE so that the use of one drug selects both ARGs together and the two types of resistance at the same time (2, 6). One example is the co-selection of resistance in response to metal-induced toxicity coupled with an antimicrobial (2, 6).

Consequences of antimicrobial resistance

The threat of antimicrobial resistance to human health has been apparent since the discovery of the first antimicrobial (7). Alexander Fleming warned about the dangers of antimicrobial resistance in his 1945 Nobel speech following his formal discovery of penicillin (7). Evidently, his warning went unheeded and antimicrobials have frequently been used without proper stewardship leading to a proliferation of resistance so that today, there are resistance mechanisms for every known drug and class of antimicrobial (4). Any use of antimicrobials can select for resistance, making their stewardship of the utmost importance for human and animal health as increased levels of resistance can negatively affect individual health outcomes, increase healthcare costs, and negatively impact the economy and the Canadian society at large (4, 8).

With the risk of having no available treatments, individual health consequences from antimicrobial resistance include an increased risk of death, increased length of illness, as well as

social and economic consequences associated with long-term illness (4, 8). The risk of acquiring a resistant infection increases with exposure to antimicrobials, but the consequences of antimicrobial resistance affect populations differently (4). Groups such as immunocompromised and elderly people often bear an increased burden of the consequences (4).

A lack of treatment options may lead to increased length of hospital stays, and with higher consequences, more healthcare resources will be required as rates of antimicrobial resistant infections increase (4, 8). The lack of treatment options is also accompanied by the demand for new treatment options to replace those that are no longer effective (4, 8). Finding, developing, and licensing new treatment options is a lengthy and highly expensive process and with every new treatment option, a resistance mechanism is likely to occur (4, 8). Antimicrobials are also used preventatively for many surgeries and medical procedures and should there be a lack of preventative treatment options the impact on patients needing invasive procedures will be larger (4). An increased burden on the healthcare system means increased costs of healthcare in Canada (4).

In addition to increased healthcare costs the economy will also be affected by antimicrobial resistance by way of increased labour shortages and increased disability-adjusted life years (4, 8). Additionally, while this will be discussed further in later paragraphs, antimicrobials are also used in agriculture, from crop production to aquaculture to food-animal production, which means resistance will also greatly impact the agricultural sector (1, 4, 9, 10). As a result, estimates of the effect of antimicrobial resistance on the Canadian economy, assuming no intervention and constant rates of resistance or rates rising to 40%, approximate a $268 to $388 billion reduction in gross domestic product (GDP) by 2050, a drop of approximately one-third of Manitoba's GDP (4). The resulting social effects of antimicrobial

resistance could include a growth in healthcare mistrust, reduced quality of life, food shortages, or increased food prices. Furthermore, since travel is a common risk factor for resistant infections this could lead to travel restrictions or a growth in xenophobia (4).

According to a recent systematic analysis, antimicrobial resistance is the leading cause of death globally and disproportionately affects low-resource areas (8, 11). In 2015, the World Health Organization made a call to action for reducing the emergence and spread of antimicrobial resistance with countries around the world committing to a Global Action Plan, and this call to action was renewed in 2021 (1). Despite the prominence of antimicrobial resistance in global policy, this activity does not appear to have translated into impact, especially in low- and middle-income countries where resources are less abundant; there has also been a noted interruption in momentum due to COVID-19 (11). In an effort to gain control of this issue and slow its spread, a number of recently published articles have investigated key intervention strategies. These suggested intervention strategies tend to fall into five main categories: infection prevention and control programs, vaccination programs, reducing non-human antimicrobial use and exposure, minimizing unnecessary antimicrobial use in human health, and investing in the development of new antimicrobials (8, 11-14). The Pan-Canadian Framework for Action has identified a number of challenges regarding these interventions such as inconsistent stewardship that tends to not extend beyond regional boundaries, insufficient investment in surveillance, and a lack of feedback and evaluation of effective interventions (15). These challenges have been echoed further by Otto et al., 2022 and 2021 (12, 13).

The importance of a One Health approach to antimicrobial resistance

Antimicrobial resistance affects the health of all sectors: human health, animal agriculture, companion animals, crop production, the health of pollinators, and aquaculture just

to name a few (1, 4, 16-19). Other considerations include how resistant bacteria are spread, whether nosocomially or by travel, through an animal or environmental vector, or even by fomite (4, 16, 20). While some of the mechanisms of antimicrobial resistance dissemination are discussed further in coming sections, antimicrobial residues and resistant organisms can persist and spread in the environment, and genes that convey resistance can also spread between organisms and within organism species (2). Even in the absence of selective pressures, resistant organisms can be found in areas where antimicrobial use has not been indicated (21). Some research suggests that only 28% of global antimicrobial resistance prevalence is attributable to antimicrobial use (22) and that political corruption, poor governance, poor infrastructure, and reduced health-care spending are better predictors for increased resistance (22, 23). Considering the complex interconnectivity of all these systems and dynamics, it is key to study antimicrobial resistance using a One Health lens which studies the intersection of humans, animals, and the environment (4, 13, 16, 24, 25).

1.1.2 *Campylobacter* spp.

What are Campylobacter*?*

Campylobacter species are a Gram-negative, motile, microaerophilic, toxin-producing bacteria consisting of around 22 different species, the two most notable and common of which in humans are *C. jejuni* and *C. coli* (26-29). Globally, *Campylobacter* are one of the leading causes of foodborne illness (26-29). Symptoms vary but often include watery diarrhea, fever, and abdominal pain (26, 27). While infections are often self-limiting and most patients will recover with supportive care and rehydration, there are rare instances of associated conditions such as: reactive arthritis (ReA), irritable bowel syndrome (IBS), Guillain-Barré Syndrome (GBS), and Miller Fisher Syndrome (MFS), a variant of GBS, which are autoimmune disorders characterized

by nerve damage, muscle weakness and sometimes paralysis (26, 27, 29). The proportion patients with *Campylobacter* infections that develop IBS has been estimated to be 4.01%, the proportion that developed ReA was 2.86%, and the proportion that developed GBS (or MFS) was 0.07%, although there are high levels of uncertainty reported with these statistics (30). Furthermore, *Campylobacter* is among the top three causes of foodborne hospitalizations along with *Salmonella* spp., verotoxigenic *E. coli*, and norovirus (31). The pathogenicity of *Campylobacter* is a result of a combination of toxin production, iron acquisition from the host, flagella-mediated mobility allowing colonization, and invasion of host cells triggering immune reactions (26, 27, 29). The most critical risk factors for *Campylobacter* infection in humans have generally been international and domestic travel followed by consumption of undercooked chicken meat or cross-contamination during food preparation, environmental exposure such as contaminated water, and contact with animals (28). Keep in mind that travel is a complex variable that is largely a proxy for a number of different, often unmeasured, factors including different water quality, differing food handling practices, and potential exposure to different pathogens (32). Regardless, risk factors for infection with *Campylobacter* spp. tend to circle back to ingesting contaminated products (28).

Poultry, especially chicken, are the most common reservoir of *Campylobacter;* other reservoirs include water, wild birds, swine, cattle, shellfish, pets, and flies (26-29). *Campylobacter* are often considered a commensal bacteria in poultry and wild birds with horizontal transmission being the most common means of spread (26-28). These sources of horizontal transmission include wild birds to farmed birds, between flocks, contaminated animal feed and water, contamination of environments surrounding poultry farms, farmers, and visitors, flies, and mealworm beetles (26-28). Hakeem et al., 2021 found that *Campylobacter* tended to

survive longer in the presence of yeasts, molds, and other microbial eukaryotes possibly by invading and replicating within these hosts, thereby cross-contaminating flocks in successive flocks (28). Besides transmission, *Campylobacter* can also spread by cross-contamination during transportation from farms to abattoirs, the abattoir processing stages, and during food-preparation (26-28). *Campylobacter* do not grow below 30˚C or above 50˚C and are unable to survive in ambient oxygen levels but can persist in suboptimal conditions, especially when moisture or a biofilm is present which means proper food handling and preparation may be a key point of intervention to prevent *Campylobacter* infection (26-28). Biofilms, a matrix of sugars, proteins, DNA, and one or more bacterial community, may contribute to the persistence and survival of *Campylobacter* outside the host and under suboptimal conditions (2, 33). The top ranked behaviours for reducing *Campylobacter jejuni* cross-contamination are: use of a thermometer to ensure adequate cooking temperature, washing surfaces and knives with hot water and soap after contact with meat, drinking pasteurized milk and juices, and washing hands with hot water and soap after handling raw meat (34). A 2017 Canadian consumer food study revealed that about 90% of Canadians self-reported taking the necessary precautions to prevent foodborne illness from raw meat (35). Unfortunately, accurate measurement of consumer compliance with proper food safety practices and behaviours is challenging (35). Other suggested key strategies include: requiring retail chicken be frozen or requiring fly screens in broiler barns (36, 37).

What are the mechanisms of antimicrobial resistance in Campylobacter?

Multiple species of *Campylobacter* display resistance to most classes of drugs due to various resistance mechanisms (5, 38). In addition to acquiring antimicrobial resistance to some antimicrobial classes, *Campylobacter* are also intrinsically resistant to a number of antimicrobial

classes such as glycopeptide and lipopeptide antibiotics (5, 38). This intrinsic resistance is likely due to the low permeability of the *Campylobacter* membrane in conjunction with multi-drug efflux pumps such as CmeABC (5, 38-40).

Campylobacter most frequently develops acquired resistance to other antimicrobial classes through chromosomal mutations that code for mechanisms rather than horizontal gene transfer (5, 38). Fluoroquinolone resistance in *Campylobacter* occurs, in part, because of a point mutation that affects the target for fluoroquinolones so that it is ineffective; the mutation is paired with an existing efflux pump, CmeABC, which works to decrease the amount of fluoroquinolone within the cell (5, 38). The point mutation occurs in the quinolone resistance-determining region of DNA gyrase A, which conveys resistance by modifying the expression of the antibiotic target (5, 38). Macrolide resistance in *Campylobacter* works similarly with a modification of the target for macrolides, either by point mutation or by adding a methyl- group (5, 38). There are three main areas of this point mutation, the most common is in the 23S rRNA, a component of the large ribosomal subunit, or the lesser occurring mutations in ribosomal proteins L4/L22 (5, 38). The same efflux pump that is responsible for removing fluoroquinolones, CmeABC, is also able to remove macrolides and tetracyclines (5, 38). Instead of point mutations, tetracycline resistance is conferred by *tet(O),* a gene that can already be part of the chromosome, or to a lesser extent can either be delivered via a plasmid, and produces proteins that structurally changes the target of tetracyclines so that they are ineffective (5, 38).

Some of these adaptations do not come at a survival cost to *Campylobacter* and result in stable, long-lasting resistance despite the removal of the antimicrobial that introduced the selective pressure (5, 38). This is particularly true for fluoroquinolone resistance in *Campylobacter* (5, 38). Chicken colonization experiments indicate that fluoroquinolone

resistance does not carry a fitness burden, and that resistant strains can outcompete fluoroquinolone susceptible *Campylobacter* and persist stably in the population after removing the antibiotic selective pressure (5, 38). Even in the absence of selective pressure from antimicrobial use, resistance genes in *Campylobacter* can spread through horizontal gene transfer mechanisms such as conjugation, spreading the genetic information needed to acquire resistance to antimicrobials (5, 38). Until recently horizontal gene transfer had not been identified as a significant contributor to resistance transmission in *Campylobacter*, as is the case for other enteric gram negative bacteria like *Salmonella* or *Escherichia coli,* but recent findings indicate that it may play a larger role than initially thought, especially in the presence of biofilms (41, 42). Biofilms also make it difficult for antimicrobial agents to reach the targeted bacteria (2). Should horizontal gene transfer of ARGs prove to be a major contributor of resistance to *Campylobacter* spp. then this would change the threat of resistance from something that is spread within *Campylobacter* spp., to something that can spread to and from *Campylobacter* spp. and other pathogens. However, these findings of horizontal gene transfer have only been investigated with chloramphenicol and kanamycin resistance (41, 42).

Why is antimicrobial resistance in Campylobacter *important?*

As with any pathogen it is important to determine whether resistance strains behave differently from susceptible strains, for example, with respect to transmission and risk factors, and if resistance is associated with an increased burden of illness. Patients with a resistant strain of *Campylobacter* can experience prolonged diarrhea, a longer duration of illness, have an increased risk of an adverse health event such as invasive illness or death, and may have a higher rate of hospitalization than a susceptible infection (43-45). In Canada, the national rate of reported *Campylobacter* infections is approximately 27.2 cases per 100,000 population (46, 47).

The reported rate of infection is likely an underestimation as those with minor symptoms may not seek care, only a proportion seeking care will have a sample tested to determine the pathogen, and not all laboratories will report cases to provincial authorities (48).

From 1999 to 2006, 37.2% of *Campylobacter jejuni* and 43.3% of *Campylobacter coli* isolates from patients in Saskatchewan were resistant to at least one class of antimicrobial (49). While levels of resistance by class varied over the study period, the class with the highest rates of resistance was frequently tetracyclines (49). The proportion of fluoroquinolone resistance was often higher in *C. coli* samples than *C. jejuni* samples, and increased from 2004 to 2006 (49). The proportion of macrolide resistance was also higher in *C. coli* than *C. jejuni* and tended to peak in 2004 (49). Lastly, while there is national reporting of human *Campylobacter* infections in Canada, there is no national testing or reporting of resistance levels in human *Campylobacter*. Aside from a handful of studies which have examined Canadian isolates, there is no ongoing surveillance (47, 49, 50). When taking into consideration the evidence of an increased burden of illness in combination with the aforementioned socio-economic consequences of antimicrobial resistance, the prevalence of *Campylobacter* in Canada, and the rates of antimicrobial resistance (46, 49), it is becoming increasingly important to understand infections with antimicrobial resistant *Campylobacter* and the dynamics of their transmission.

Antimicrobial use and resistance in Campylobacter *in chicken in Canada*

Food is a common source of human *Campylobacter* infection, with chicken meat in particular, being a major source (27, 29, 51). The Canadian National Microbiological Baseline Study of Broiler Chicken which ran from 2012-2013 puts the national prevalence of *Campylobacter* in broiler chickens, sampled from whole carcasses, at 24.1%, with British Columbia reporting the highest prevalence at 41.3% (52). More recent data indicate that

nationally, 40.8% of *Campylobacter* isolates from broiler chicken are resistance to at least one antimicrobial class (53). Since antimicrobial use is the strongest driver of antimicrobial resistance emergence, the Chicken Farmers of Canada have implemented plans to phase out the preventative use of antimicrobials important to human medicine in broiler chicken production (2, 4, 54). Following the ban on preventative use of category I antibiotics for chicken in 2014, which includes fluoroquinolones, in 2017, restrictions were placed on Canadian chicken farmers to ban the preventative use of category II antimicrobials, which include macrolides and quinolones (54). They are currently working towards a ban on the preventative use of category III antimicrobials, which include tetracyclines (54). As of December 2018, the Government of Canada has restricted use of all Medically Important Antimicrobials in animals to be under veterinary prescription only (55, 56). This restriction is also in place with the Chicken Farmers of Canada who also only support using these antimicrobials of very high, high, and medium importance to human health by prescription only (54). Although fluoroquinolone use is allowed therapeutically in chicken production, there are no approved products for poultry use in Canada and any use is therefore off-label use and requires a valid veterinarian-client-patient relationship; this includes off-label use for metaphylaxis (Dr. Agnes Agunos, Public Health Agency of Canada, personal communcation, October-December 2021) (57). Even with the ban, interventions to the prevention of infection can also contribute to reducing the use of antimicrobials; these include improved animal husbandry practices such as improved ventilation, improved sanitation, vaccination, and reducing cross-contamination between flock turnovers (9, 28, 54, 58).

1.1.3 Surveillance of Antimicrobial Resistance in Canada

Surveillance data is key in quantifying, monitoring, and tracking antimicrobial resistance in addition to guiding policy and identifying areas for interventions (13, 16). The Public Health

Agency of Canada has a national antimicrobial resistance surveillance program, the Canadian Antimicrobial Resistance Surveillance System (CARSS), launched in 2015, which incorporates a summary of data from a number of sector-specific programs. These programs include the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS), initiated in 2002, which conduct surveillance on foodborne antimicrobial resistance in the food chain (food animals, food, and humans) and antimicrobial use in animals, and the Canadian Nosocomial Infection Surveillance Program (CNISP), initiated in 1994, which conducts surveillance of antimicrobial resistant nosocomial infections, primarily in tertiary referral hospitals (59). The CIPARS program incorporates data on antimicrobial use in crops from the Pest Management Regulatory Agency and in aquaculture form the Department of Fisheries and Oceans (18). In addition to CIPARS and CNSIP, CARSS includes data from seven other PHAC surveillance systems and collects data on antimicrobial use in humans (13). However, CARSS and its current components do not encompass the full scope of antimicrobial resistance and use in Canada (13, 16). Gaps in surveillance include but are not limited to: full integration of data, limited data on resistance in companion animals and the associated risks, up-to-date resistance prevalence estimates for sectors outside of the main livestock groups, limited or no data on resistance in animal pathogens, a lack of data for the many regions in Canada, and limited data for non-hospitalized patients (13, 16). A recent evaluation of integrated, One Health surveillance of antimicrobial use and resistance in Canada aimed to assess the current state of these surveillance programs in Canada and recommended three critical areas to focus attention which were: increased resources for antimicrobial resistance and use surveillance, policies that standardize reporting of resistance and antimicrobial use across jurisdictions, and the development of a complete and fully integrated surveillance program across One Health sectors (12-14).

Despite the strong link of human foodborne illness to food-producing animals, the link between antimicrobial resistance in animals and resistance in humans is more complex (60). Resistant bacteria can be exchanged between livestock and farm workers but there is less evidence of direct transmission from food to the general population (60). The reasons for this are complex but there is a growing body of research using genomics and bioinformatics to track the transmission of resistance from food, although this is mostly for *Salmonella* (61). Furthermore, since most foodborne illnesses should not be treated with antimicrobials, the lack of selective pressure may favour susceptible bacteria over the resistant bacteria, especially for resistance mechanisms that result in a fitness burden (62). An additional consideration is that the risk of transmission can be reduced if animal products are handled and prepared according to food safety guidelines (60). Clarifying the transmission pathway between animals and humans will not only allow us to quantify the risk to humans from animals but will also allow us to identify areas of intervention and prevention. There are a number of possible ways to model this transmission pathway, these include but are not limited to: quantitative microbial risk assessments, agent-based modelling, and integrated assessment models (63-66).

Following the call from the World Health Organization urging countries to implement antimicrobial resistance surveillance and for that surveillance to include the food animals and foodborne antimicrobial resistance, CIPARS was initiated in the early 2000s (18). CIPARS is the only surveillance system for antimicrobial use and resistance in Canada that was designed with a One Health approach to represent farm-to-fork surveillance of foodborne antimicrobial resistance and animal antimicrobial use (13). In order to be better able to interpret CIPARS and other antimicrobial resistance surveillance data related to foodborne resistance in the broader context and with respect to potential resistance mitigation interventions, an integrated assessment model

for antimicrobial resistance (iAM.AMR) has been developed (67). Integrated assessment models, used for other complex systems like climate change research (9, 68), are a useful tool for understanding antimicrobial resistance since they provide a structured process for incorporating knowledge from various disciplines about complex issues in order to produce integrated insights for decision-makers (68). Currently the model incorporates chicken, cattle, and swine transmission pathways mainly for *E. coli* and *Salmonella*, and resistance to tetracyclines, macrolides, quinolones, and third generation cephalosporin drug classes (9, 67). The integrated assessment model utilizes factor data from peer-reviewed articles, prevalence data from CIPARS and other surveillance programs, national food consumption data, and expert opinion (67). To date, the model does not include the *Campylobacter*-chicken pathway from farm to retail for any drug class. Additionally, the model has not been taken beyond the retail step to assess the impact of human exposure, the consequences of antimicrobial resistance in the course of foodborne or other illness.

1.2 Research Objectives

To better understand the dissemination of antimicrobial resistant *Campylobacter,* the overall objective of this thesis was to investigate the human exposure to, and risk from, antimicrobial resistant *Campylobacter* in Canada. In addition to investigating transmission pathways in general, because of the contribution of chicken meat to *Campylobacter* spread, this thesis also investigated the potential exposure from broiler chickens. The overall objective was broken down into two main research questions and objectives:

1. Which factors are associated with antimicrobial resistant *Campylobacter* infections in humans?

Objective: To determine factors potentially associated with human infection with *Campylobacter* spp. that are resistant to fluoroquinolones, macrolides, or tetracyclines.

2. What is the probability of exposure to antimicrobial resistant *Campylobacter* from broiler chickens and chicken meat in Canada from farm to retail?

   Objective: To develop an integrated assessment model component to evaluate the probability of human exposure to antimicrobial resistant *Campylobacter* spp. from broiler chicken in Canada resistant to fluoroquinolones, tetracyclines, or macrolides and identify knowledge and data gaps.

CHAPTER 2: A SCOPING REVIEW OF FACTORS ASSOCIATED WITH ANTIMICROBIAL RESISTANT *CAMPYLOBACTER* SPP. INFECTIONS IN HUMANS

Abstract

Campylobacter spp., a leading cause of acute diarrheic illness in humans around the world, have developed resistance to antimicrobials important for human medicine. Infection with antimicrobial resistant *Campylobacter* spp. is an important public health concern as antimicrobial resistance (AMR) has been linked with increased severity of illness and risk of death. The objective of this study was to perform a scoping review of factors associated with human infection with antimicrobial resistant *Campylobacter*.

Comprehensive literature searches were performed in five primary and three grey literature databases. Criteria for inclusion were analytical English publications investigating humans infected with a *Campylobacter* strain resistant to macrolides, tetracyclines, fluoroquinolones, and/or quinolones that reported factors potentially linked with the infection. Primary and secondary screening were completed independently by two reviewers using Distiller SR®.

The search identified 8,527 de-duplicated articles and 27 articles were included after screening. Factors were broadly categorized into seven categories: animal contact, prior antimicrobial use, participant characteristics, food and food preparation, travel, underlying health conditions, and water. Articles exploring factors related to travel (n=17) and participant characteristics (n=14) were most common. The factors and regions studied, the types of investigations, and the knowledge they contributed are broad and diverse. The populations included, data sources utilized, and analyses employed varied greatly. Travel was an important risk factor, and infections were commonly associated with gastrointestinal *Campylobacter jejuni*

and were often evaluated using only a univariable analysis. Most of the studies were conducted in a small sample of high-income, westernized countries.

This scoping review mapped current literature investigating factors related to antimicrobial resistant *Campylobacter* infections in humans. The heterogeneity of the results and articles provided a broad overview of the available factors while also illuminating areas for potential future research.

2.1 Background

2.1.1 Rationale

Risk Factors for Campylobacter in General

Campylobacter spp. is one of the leading causes of acute diarrheic illness, accounting for 16% of foodborne illness globally (69) and 8.42% of foodborne illness in Canada (48). Infections are characterized by acute, watery diarrhea progressing to bloody diarrhea and often accompanied by abdominal pain, but vomiting is uncommon (51). *Campylobacter* infection has an incubation period of 2-4 days and most people recover within 2-5 days (70). An uncomplicated infection typically only requires supportive care to avoid dehydration (70); however, some cases develop bacteremia (71). Although uncommon, complications related to *Campylobacter* include but are not limited to: reactive arthritis (ReA), irritable bowel syndrome (IBS), Guillain-Barré Syndrome (GBS), and Miller Fisher Syndrome (MFS), a variant of GBS, which are autoimmune disorders characterized by nerve damage, muscle weakness and sometimes paralysis (26, 27, 29, 71).

Antimicrobials in the macrolide and quinolone family are sometimes used in the treatment of complicated *Campylobacter* infections and have been indicated to reduce duration of illness (72), providing that the infection is susceptible to these antimicrobials. However, resistance to macrolides, fluoro(quinolones), and other antimicrobial classes including tetracyclines, is not rare (5). There is evidence that inappropriate antimicrobial prescribing practices occur in Canada when it comes to *Campylobacter* spp. infections, such as: prescribing antimicrobials after symptoms have resolved, or before the culture results have confirmed the diagnosis of *Campylobacter*, and even treatment before the collection of a sample (50). Furthermore, antimicrobials not suggested by prescribing guidelines have also been prescribed

(73). Antimicrobial resistance is the ability of a microorganism to stop an antimicrobial from working against it, rendering standard treatments ineffective (1). Patients with a resistant strain of *Campylobacter* may have an increased risk of an adverse health event such as a longer duration of illness, hospitalization, invasive illness or death, than patients with a susceptible infection (43, 45, 74).

Some known risk factors associated with *Campylobacter* spp. infections in general include: undercooked meat, especially chicken, contaminated unpasteurized milk, animal contact, and contaminated water (70). There is a relatively large amount of research on factors associated with *Campylobacter* infections; however, a search on January 21, 2020 in Ovid Medline®, Cochrane Library, Joanna Briggs Institute Systematic Review Registry, and Google Scholar did not reveal any scoping or systematic reviews on factors associated with antimicrobial resistant *Campylobacter* infections.

2.1.2 Objective

The objective of this scoping review is to synthesize the available, globally published literature on factors associated with human infections and antimicrobial resistant *Campylobacter* species. The antimicrobials of interest for this scoping review were: macrolides, tetracyclines, fluoroquinolones and/or quinolones.

2.2 Methods

2.2.1 Protocol and registration

The review followed the Joanna Briggs Institute framework (75) as well as the PRISMA Scoping Review guidelines (76). The protocol was registered with the Joanna Briggs Institute Systematic Review Register on February 5, 2020.

2.2.2 Eligibility criteria

The review included any analytic study, which was generally defined as a study that used a comparison group, including theses and dissertations. Study designs or publications that were excluded from the review were: review articles, commentaries, opinion pieces, editorials, newspaper articles, books, book chapters, and conference proceedings. There were no limits applied to language, geographical location, *Campylobacter* species, and date of publication. However, due to a lack of translation resources, non-English articles that were identified during primary screening were excluded from this review.

Any study that evaluated humans of any age with a *Campylobacter* spp. infection (confirmed by recognized laboratory methods) were included. Non-human research, studies that evaluated infections other than *Campylobacter*, studies that evaluated colonization instead of infection, and studies that failed to confirm a *Campylobacter* infection by recognized laboratory methods were excluded.

Studies also needed to evaluate an exposure of interest, including factors involved with a human infection with a resistant *Campylobacter* strain. These factors include but are not limited to: age, recent travel, or pre-existing medical conditions. Studies that did not evaluate factors related to a human infection were excluded. The comparator group had to be appropriate to the study design. For example, when applicable, the comparator group for case-control studies were infections with *Campylobacter* that are susceptible to the antimicrobials of interest. Studies had to include the outcome of interest, namely infection with *Campylobacter* resistant to the antimicrobials of interest: macrolides, tetracyclines, and fluoro(quinolones). Resistance had to be determined by recognized laboratory antimicrobial susceptibility testing methods such as disk diffusion or broth micro-dilution.

2.2.3 Information sources

Databases included: MEDLINE® in Ovid, AGRICOLA™ in ProQuest®, Centre for Agriculture and Bioscience abstracts in Web of Science, EMBASE® in Ovid, and Scopus®. Grey literature sources included: World Health Organization's Global Index Medicus, and the Bielefield Academic Search Engine. Additionally, the first 250 results, sorted based on relevance, from Google Scholar were included.

2.2.4 Search

The search string was developed based on eligibility criteria with the assistance of a research librarian, beginning with an initial limited search in Ovid MEDLINE® using a preliminary search string. Following an informal analysis of terms used in the title, abstract, and index, relevant terms were included in the search string. Next, the search string was adapted (see Appendix 2.1) and applied across the remaining information sources. Articles were de-duplicated in three stages in Mendeley (*Mendeley,* Version 1.19.8. Elsevier; 2021), EndNote (*EndNote*, Version X9.2. Clarivate Analytics; 2018), and DistillerSR (*DistillerSR*. Version 2.35. Evidence Partners; 2021.). The search was completed on February 5, 2020 following the confirmation of protocol registration. The search was updated on May 7, 2021.

2.2.5 Selection of sources of evidence

Primary and secondary screening were completed by two independent reviewers. Primary screening involved reviewing the title and abstract of each article and followed the primary screening decision tree found in Appendix 2.1. The possible answers were yes, no, or unclear. Articles proceeded to secondary screening if all questions were answered with a yes or unclear from both reviewers. Reviewers met to resolve conflicts if there was a disagreement about whether to include the article. The secondary decision tree was followed for secondary screening (see Appendix 2.1) and answers were based on review of the full text articles, if they could be

located. After initially testing the secondary screening form on ten articles, questions were rearranged to streamline the screening process by moving the article type question to the first question position. Questions only had yes or no response options and an article was included if all questions were answered with yes. The reasons for exclusion were documented.

2.2.6 Data collection and synthesis

The data extraction form was designed with input from the project team so that extracted data could be linked for further research (see Appendix 2.3). Extracted data included: characteristics of the study, characteristics of the study participants, and a description of and results for factors investigated in the study. Initially, the form was tested on five articles and adjustments were made before extracting all articles. Data were extracted by one reviewer in Distiller SR and exported into Excel for cleaning.

Results were synthesized into tables, figures, and qualitative findings to present an effective comprehensive narrative of the research.

2.3 Results

2.3.1 Selection of sources of evidence

The search identified 8,527 de-duplicated articles. Of these, 8,089 articles were excluded during primary screening and an additional 411 additional articles were excluded during secondary screening, including 12 articles that we were unable to locate a full-text pdf despite inter-library loan requests (Figure 2.1). Twenty-seven articles met all inclusion criteria and were included in the review.

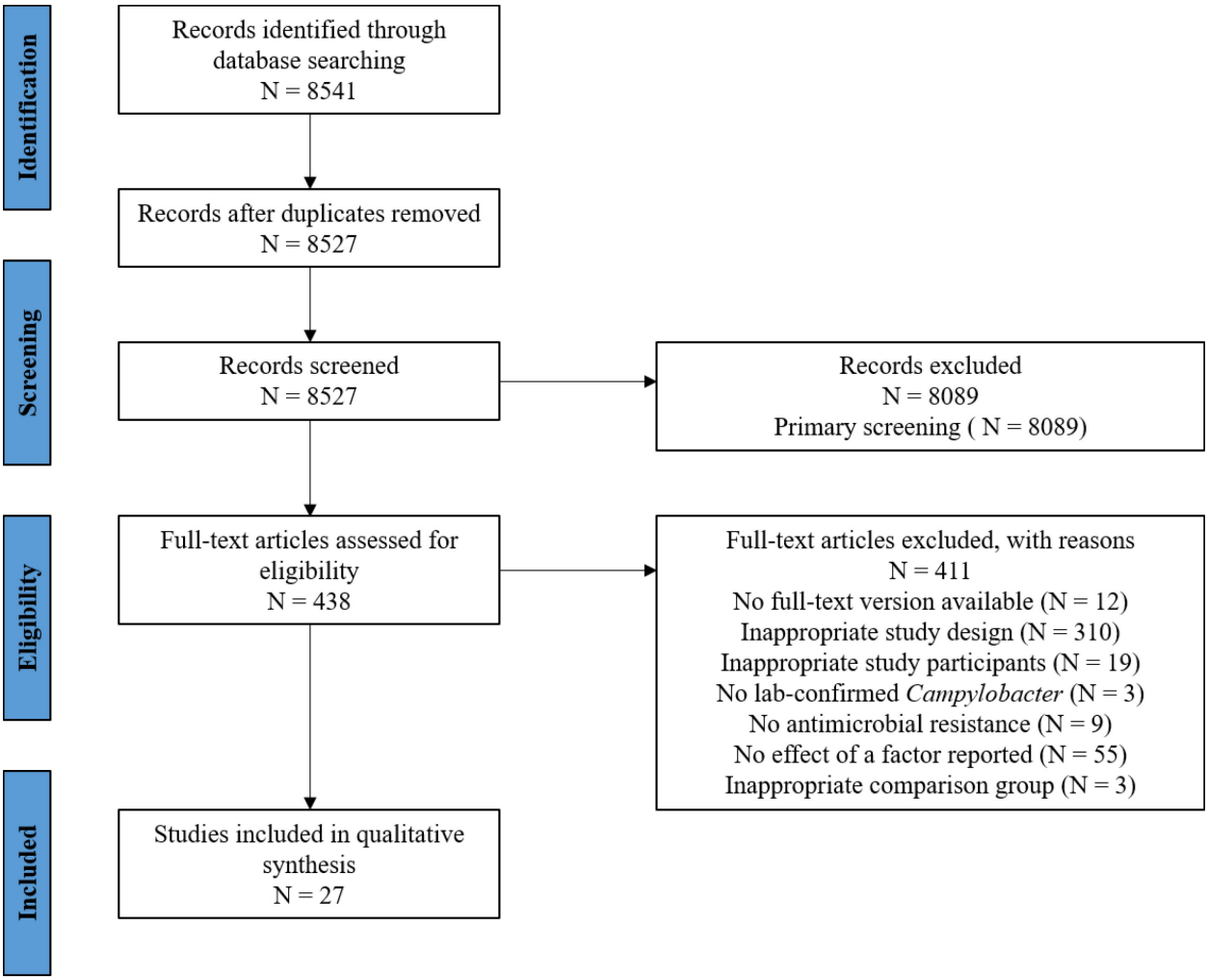


Figure 2.1. PRISMA-ScR flow diagram of the study selection process for the scoping review of human infection with antimicrobial resistance *Campylobacter*.

2.3.2 Characteristics of sources of evidence

An overview of the characteristics of included articles can be found in Table 2.1. All articles were published between the years of 1998 and 2018 with the exception of one article that was published in 1988. The most common countries that data were collected from included: the United States (six articles), Denmark (four articles), Canada (three articles), and the United Kingdom (three articles). Study designs were primarily cross-sectional (n=12) and case-control/comparison (n=9). The average age of participants in most studies was between 20 and

50 but variations in reporting age details made summarizing age characteristics difficult. Out of the 27 studies, some either did not specify gender or sex of participants (n=9) or did not include females in their study (n=4). The majority of the articles studied gastrointestinal infections (n=19, 70.4%), and focused on or included data for *Campylobacter jejuni* (n=22, 81.5%). Most studies determined resistance to multiple antimicrobials: 74.1% of articles (n=20) studied resistance to fluoroquinolones, 33.3% (n=9) studied resistance to quinolones, 48.1% (n=13) studied macrolide resistance, and 25.9% (n=7) studied tetracycline resistance. There was a four article overlap that included data on resistance to both quinolones and fluoroquinolones.

Table 2.1. Key characteristics of peer-reviewed references included in the scoping review of factors related to human infection with antimicrobial resistant *Campylobacter* spp.

Author	Year	Study Design [a]	Location	Total Sample Size	Female (%) [b]	Age Details (years) [c]	AMR [d]	Species	Infection Type [e]
Bottieau, E et al. (77)	2011	Prospective cohort	Belgium	1730	NS	Mean = 33 Range = <1-73	FLQ	*jejuni*	GI
Engberg, J et al. (45)	2004	Case-control	Denmark	126	83.3	Mean = 33 IQR = 20-45	QL FLQ	*jejuni*	NS
Evans, M et al. (78)	2009	Case-control	United Kingdom	556	50.7	Med (cases) = 53 Med (comp.) = 49	FQL	NS	NS
Feodoroff, B et al. (79)	2010	Cross-sectional	Finland	166	59.6	NS	FQL	*jejuni*	GI
Gallay, A et al. (80)	2007	Case-case-control	France	570	0	Mean (cases) = 19.5 Mean (cont.) = 20	FQL	*jejuni*, *coli*, *fetus*, *lari*	GI
Gaudreau, C et al. (81)	2003	Retrospective cohort	Canada	14	0	Range = 26-40	MCL FQL TET	*jejuni*	GI
Gaudreau, C et al. (82)	2015	Retrospective cohort	Canada	31	0	Range = 21-64	QL FQL TET	*jejuni*	GI
Ghunaim, H et al. (83)	2015	Cross-sectional	United Kingdom	174	40.2	Med. = 2 Range = <1-75	MCL FQL	*jejuni*	GI
Hakanen, A et al. (84)	2003	Cross-sectional	Finland	354	NS	NS	FQL	*jejuni*	GI
Helms, M et al. (43)	2005	Cohort	Denmark	3541	NS	Mean = 27.4 Range = 0.2-92.3	MCL QL	NS	GI
Jenkin, G et al. (85)	1998	Cross-sectional	Australia	20	10.0	Mean = 40 Range = 27-53	FQL	*upsaliensis*	GI

Johnson, J et al. (86)	2008	Case-control	Canada	210	45.2	16+	FQL	*jejuni*, *coli*, NS	NS
Koningstein, M et al. (87)	2011	Cross-sectional	Denmark	10475	NS	Range = 0-80+	MCL FQL	NS	GI
Kownhar, H et al. (88)	2007	Case-Control	India	400	41.8	Mean (cases) = 37 Mean (cont.) = 39.3	MCL QL FQL TET	*jejuni*	GI
Lu, P et al. (89)	2000	Retrospective cohort	Taiwan	21	42.9	Med. = 45 Range = 4-81	MCL	*jejuni*, *coli*	BS
Nelson, J et al. (44)	2004	Case-control	United States	740	46.0	Med. = 34 Range = <1-96	FQL	NS	GI
Patrick, M et al. (90)	2018	Cross-sectional	United States	16549	45.0	Med. = 38	MCL QL	*jejuni*	Both
Perlman, D. M. et al. (91)	1988	Cohort	United States	4	0	Mean = 47 Range = 39-67	MCL	*jejuni*, *coli*	GI
Ricotta, E et al. (92)	2014	Cross-sectional	United States	24433	45.5	Mean (cases) = 37.1 Mean (comp.) = 36.2	MCL QL	Mostly *jejuni*	GI
Sharma, H et al. (93)	2003	Case-control	Australia	155	NS	NS	MCL QL FQL TET	*jejuni*	GI
Skjot-Rasmussen, L et al. (94)	2009	Cross-sectional	Denmark	1023	NS	NS	MCL QL TET	*jejuni*	NS
Smith, K E et al. (95)	1999	Case-control	United States	390	NS	NS	QL	*jejuni*	GI

Moore, J E et al. (96)	2002	Cross-sectional	Ireland	15	26.7	Mean = 29.4 Range = 1-67	FQL TET	15 *jejuni*, 2 *coli*	GI
Uzunovic-Kamberovic, S et al. (97)	2009	Cross-sectional	Bosnia and Herzegovina	2491	NS	Med. range = 0-6 Range = 0-64+	MCL FQL	*jejuni*, *coli*	GI
CSSSC [f], Painter, M J et al. (98)	2002	Case-control	United Kingdom	495	52.3	Mean (cases) = 39 Mean (cont.) = 38	FQL	*jejuni*	GI
WonHee, C et al. (99)	2016	Cross-sectional	United States	94	42.9	Med. = 23.5 Range = <2-50+	FQL	*jejuni*	NS
van Hees, B et al. (100)	2006	Cross-sectional	Netherlands	18856	NS	NS	MCL FQL TET	94% *jejuni*	NS

[a] When a study design was not specified by the authors, a study design was assigned during data extraction
[b] % female vs other, specified in article or calculated during data extraction where possible, NS=Not specified
[c] Specified in article or calculated during data extraction where possible, IQR= interquartile range, Med.=Median, cont.=controls, comp.=comparisons, NS=Not specified
[d] Antimicrobial Resistance, MCL=Macrolides, QL=Quinolones, FQL=Fluoroquinolones, TET=Tetracyclines
[e] Specified in article or determined during data extraction where possible, GI=Gastrointestinal Infection, BS=Blood-stream infection, NS=Not specified/could not be determined
[f] CSSSC= *Campylobacter* Sentinel Surveillance Scheme Collaborators

2.3.3 Results of individual sources of evidence

Factors related to antimicrobial resistant *Campylobacter* spp. infections investigated from the 27 articles are summarized in Table 2.2 and can be broadly categorized into seven categories: animal contact (Table 2.3), prior antimicrobial use (Table 2.4), participant characteristics (Table 2.5), food and food preparation (Table 2.6), travel (Table 2.7), underlying health conditions (Table 2.8), and water (Table 2.9). Articles exploring factors related to travel (n=17) and participant characteristics (n=14) were most common. Odds ratios with a value less than one are associated with lower odds of the outcome of infection with an antimicrobial resistant *Campylobacter*, while odds ratios with values greater than one are associated with higher odds of the outcome (101) for a given factor. In this context, when comparing resistant infections to susceptible infections, an odds ratio with a value of less than one is generally considered a protective factor while a value greater than one is generally considered a risk factor.

Table 2.2. Factors investigated related to antimicrobial resistant *Campylobacter* spp. infections in humans identified in studies included in the scoping review*.

Category	Factor	# of relevant articles	Reference
Animal Contact		**5**	
	Unspecified	1	(45)
	Pets	4	(78, 95, 98, 99)
	Zoo animals	1	(78)
Prior Antimicrobial Use		**7**	
		7	(45, 78, 80, 86, 89, 93, 95)
Characteristics		**13**	
	Age	8	(78, 83, 86, 87, 90, 97-99)
	Contact with children	1	(78)
	Education	3	(44, 78, 86)
	Employment status	2	(78, 98)
	Gender/Sex	6	(44, 78, 83, 86, 96, 99)
	Geography	3	(44, 86, 90)
	Income	1	(44)
	Men who have sex with men	2	(81, 82)
	Race	2	(44, 90)
	Season of infection	3	(86, 98, 99)
	Species of *Campylobacter*	2	(86, 90)
	Year of collection	1	(84)
Food and Food Preparation		**4**	
	Baby food	1	(98)
	Barbequed	1	(98)
	Beef	1	(45)
	Chicken	4	(45, 78, 98, 99)
	Cold cuts	2	(78, 98)
	Eggs	1	(78)
	Eating away from home	2	(78, 98)
	Fish and shellfish	1	(98)
	Handling of raw chicken	1	(78)
	Handling of raw meat	1	(45)
	Lamb or mutton	1	(78)
	Organic Vegetables	1	(98)
	Pate	1	(98)
	Pork	1	(78)
	Poultry (excl. chicken or turkey)	1	(45)
	Sausages	2	(45, 98)

	Storing raw chicken in fridge	1	(78)
	Unpasteurized milk	1	(78)
Travel		**16**	
	Africa	4	(77, 83, 92, 98)
	Arabian Peninsula	1	(83)
	Asia	6	(77, 83, 84, 92, 95)
	Australia/New Zealand	1	(98)
	Europe	5	(78, 84, 92, 95, 98)
	Ill contact who traveled	1	(78)
	Travel (general)	13	(43-45, 78, 79, 86, 90, 93-95, 98-100)
	Latin America	2	(77, 98)
	North Africa-Middle East	1	(77)
	North America	2	(95, 98)
Underlying Conditions		**5**	
	Antacid use	1	(78)
	Diabetic	1	(78)
	HIV	3	(85, 88, 91)
	Unspecified	1	(44)
Water		**4**	
	Bottled water	2	(78, 98)
	Filtered jug water	1	(98)
	Private water supply	1	(98)
	Public water supply	2	(45, 98)
	Sparkling bottled water	1	(78)
	Swimming	3	(45, 95, 98)
	Tap water	1	(78)
	Untreated water	1	(95)

*This table includes factors that were investigated, regardless of statistical significance.

2.3.3 Synthesis of results

Animal contact

Four articles explored the effects of animal contact on resistant *Campylobacter* spp. infections (45, 78, 98, 99). The significance and direction of the association between animal contact and a resistant infection varied between the five articles (Table 2.3). Outside of contact with zoo animals, animal contact was indicated as a protective factor (45, 78, 98, 99).

Prior Antimicrobial use

Seven distinct articles explored the effect of prior antimicrobial use on resistant *Campylobacter* spp. infections (Table 2.4) (45, 78, 80, 86, 89, 91, 95). Statistically significant risk factors for a resistant infection included: possession of non-prescribed antibiotics (86) and use of an antibiotic before specimen collection (45, 95), but results were variable and inconsistent. Five of the seven articles defined the interval for prior antimicrobial use as a month, or four weeks (45, 78, 80, 93, 95) and the start point of this interval included a month prior to: onset of illness (80, 95), onset of symptoms (45), infection (93), or stool sample (86).

Characteristics

Fourteen articles (51.9%) explored factors related to participant characteristics such as age, season of infection acquired, or level of education (44, 78, 81-84, 86, 87, 90, 96-99). The significance and direction of these association varied among the articles (Table 2.5). Only four articles conducted analyses on their data (78, 90, 98, 99). Summer was indicated as a protective factor (98, 99), while the odds of infection with resistant *Campylobacter* spp. infection increased with age (78, 90, 98, 99).

Food and Food Preparation

Four articles investigated factors related to food and food preparation (Table 2.6) (45, 78, 98, 99). Similar to patient characteristics and animal contact factors, direction of the association between the food factors and their significance varied greatly between the articles. Results from multivariable analyses even provided opposing results for factors such as chicken consumption (45, 98).

Travel

Sixteen out of the twenty-seven articles (59.3%) investigated factors related to travel and its effect on risk of a resistant *Campylobacter* infection (Table 2.7) (44, 45, 77-79, 83, 84, 86, 90, 93-95, 98-100). Nine explored foreign travel in general and all articles found it to be a statistically significant risk factor for a resistant infection (44, 45, 78, 90, 92, 93, 95, 99, 100). Evans et al. 2009 looked at food and water exposure during travel, both international and domestic, but did not evaluate travel type as a possible interaction in their analysis (78). Quantifying the comparison group for travel-related factors was difficult because it varied from study to study. As a result, it was challenging to identify specific travel locations associated with resistant infections.

Underlying conditions

Five studies explored factors related to underlying health conditions and their effect on the risk of a resistant *Campylobacter* spp. infection (Table 2.8) (44, 78, 85, 88, 91). Two of these studies completed analyses on their data (44, 78) and the only statistically significant factor was a protective effect for those with diabetes (78).

Water

Four articles explored factors related to water and infections from resistant versus susceptible *Campylobacter* (Table 2.9) (45, 78, 95, 98). Due to varying water qualities in different countries, we included the country of water origin where possible for context. While most factors included were statistically significant, direction and size of effect of factors varied among articles.

Table 2.3. Key data extracted for animal contact factors identified in studies included in the scoping review for human infection with antimicrobial resistant *Campylobacter* species isolates compared to susceptible isolates, sorted by ascending univariable result.

Reference	Study Design[a]	Factor	Species[b]	AMR[c]	Univariable Result*	Multivariable Result*
(78)	Case-control	Domestically acquired infection: own rabbit or guinea pig	NS	FQL	OR = 0.0 (0.0-0.7), p=0.01	N/A
(98)	Case-control	Contact with a pet hamster	J	FQL	OR = 0.10 (0.01-0.90), p=0.0106	N/A
(98)	Case-control	Indigenous[d] acquired: contact with a pet guinea pig	J	FQL	OR = 0.21 (0.03-1.57), p=0.09	N/A
(98)	Case-control	Contact with a pet bird	J	FQL	OR = 0.21 (0.06-0.75), p=0.0078	OR = 0.11 (0.02-0.58), p=0.009
(95)	Case-control	Contact with pets	J	QL	OR = 0.3 (0.2-0.6), p<0.001	N/A
(99)	Cross-sectional	Domestic animal contact	J	FQL	OR = 0.37 (0.10-1.33), p=0.19	OR = 0.26 (0.041-1.659), p=0.1542
(98)	Case-control	Contact with a pet rodent	J	FQL	OR = 0.38 (0.12-1.20), p=0.0864	N/A
(45)	Case-control	Animal contact	J	FQL	OR = 0.44 (0.20-0.94), p=0.032	N/A
(98)	Case-control	Contact with animals	J	FQL	OR = 0.52 (0.34-0.77), p=0.0011	N/A
(78)	Case-control	Own any pets	NS	FQL	OR = 0.6 (0.4-0.8), p=0.003	N/A
(98)	Case-control	Contact with a pet dog	J	FQL	OR = 0.65 (0.39-1.07), p=0.0883	N/A
(78)	Case-control	Contact with zoo animals	NS	FQL	OR = 5.8 (1.2-36.2), p=0.01	N/A

[a]Study design was either specified by author or designated during data extraction
[b]*Campylobacter* species; NS=Not specified, J=*jejuni*, C=*coli*, F=*fetus*, L=*lari*, U=*upsaliensis*, O=other
[c]FQL=Fluoroquinolones, MCL=Macrolides, QL=Quinolones, TET=Tetracyclines, [d]The term 'Indigenous' was the term used in the source text and can be considered synonymous with domestic acquisition (i.e., not obtained during travel)
*Per the scoping review protocol, data were only extracted if results compared resistant to susceptible. Data include the estimate of the measure of association from the model (OR = odds ratio), the 95% confidence interval in brackets, and the p-value.

Table 2.4. Key data extracted for prior antimicrobial use factors identified in studies included in the scoping review for human infection with antimicrobial resistant *Campylobacter* species isolates compared to susceptible isolates, sorted by ascending univariable result.

Reference	Study Design[a]	Factor	Species[b]	AMR[c]	Univariable Result*	Multivariable Result*
(89)	Retrospective Cohort	Appropriate vs inappropriate antimicrobial agents	JC	MCL	No analysis	
(91)	Cohort	Erythromycin use and HIV	JC	MCL	No analysis	
(78)	Case-control	Antibiotic use in the previous month	NS	FLQ	OR = 0.8 (0.3-1.9), p=0.77	N/A
(80)	Case-case-control	Association between use of antibiotics in the month before disease onset and ciprofloxacin-resistant *Campylobacter* infection in a case-control study by species	JCFL	FLQ	OR = 1.5 (0.7-3.5)	N/A
(80)	Case-case-control	Association between use of antibiotics in the month before disease onset and ciprofloxacin-resistant *Campylobacter* infection in a case-control study by species	J	FLQ	OR = 2.3 (0.9-5.8)	N/A
(45)	Case-control	Fluoroquinolone treatment after illness onset but before stool sample or 4 weeks before symptom onset	J	FQL	OR = 4.44 (1.15-17.09), p=0.031	N/A
(86)	Case-control	Possession of non-prescribed antibiotics: participant possessed antibiotics that were not prescribed for them that were saved for future use	JCO[d]	FLQ	OR = 4.8 (1.3-17.1), p<0.05	OR = 13.3 (2.2-80.9), p=0.005
(95)	Case-control	Use of a quinolone before the collection of stool specimens	J	QL	OR = 7.4 (3.1-20.3), p<0.001	OR = 7.5 (2.6-21.3), p<0.001

[a]Study design was either specified by author or designated during data extraction
[b]*Campylobacter* species; NS=Not specified, J=*jejuni*, C=*coli*, F=*fetus*, L=*lari*, U=*upsaliensis*, O=other, [d]other, as specified in the text
[c]FQL=Fluoroquinolones, MCL=Macrolides, QL=Quinolones, TET=Tetracyclines

*Per the scoping review protocol, data were only extracted if results compared resistant to susceptible. Data include the estimate of the measure of association from the model (OR = odds ratio), the 95% confidence interval in brackets, and the p-value.

Table 2.5. Key data extracted for factors related to patient characteristics identified in studies included in the scoping review for human infection with antimicrobial resistant *Campylobacter* species isolates compared to susceptible isolates, sorted by ascending univariable result.

Reference	Study Design[a]	Factor	Species[b]	AMR[c]	Univariable Result*	Multivariable Result*
(84)	Cross-sectional	Difference between two study periods: 1995-1997 (comparison group) compared to 1998-2000 (exposed group)	J	FQL	No analysis	
(83)	Cross-sectional	Gender: male vs female	J	FQL	No analysis	
(83)	Cross-sectional	Gender: male vs female	J	MCL	No analysis	
(83)	Cross-sectional	Age class	J	MCL	No analysis	
(83)	Cross-sectional	Age class	J	FQL	No analysis	
(87)	Cross-sectional	Age group by class of drug	NS	FQL	No analysis	
(87)	Cross-sectional	Age group by drug class	NS	MCL	No analysis	
(81)	Retrospective cohort	Men who have sex with men (MSM)	J	MCL	No analysis	
(81)	Retrospective cohort	MSM	J	TET	No analysis	
(81)	Retrospective cohort	MSM	J	FQL	No analysis	
(82)	Retrospective cohort	MSM	J	FQL	No analysis	
(82)	Retrospective cohort	MSM	J	QL	No analysis	
(82)	Retrospective cohort	MSM	J	FQL	No analysis	
(82)	Retrospective cohort	MSM	J	TET	No analysis	
(85)	Cross-sectional	HIV	U	FQL	No analysis	
(96)	Cross-sectional	Gender/sex: male vs not male	JC	TET	No analysis	
(96)	Cross-sectional	Gender/sex: male vs not male	JC	FQL	No analysis	
(97)	Cross-sectional	Age group of 20-64 compared to the age group of 0-6	JC	MCL	No analysis	
(97)	Cross-sectional	Age group of 20-64 compared to the age group of 0-6	JC	FQL	No analysis	

(86)	Case-control	Sex: female vs male	JCO	FQL	No analysis	
(86)	Case-control	Age, 4 categories= <28, 28-37, 38-49, 50+	JCO	FQL	No analysis	
(86)	Case-control	College or university education	JCO	FQL	No analysis	
(86)	Case-control	Season of reported infection	JCO	FQL	No analysis	
(86)	Case-control	Health region	JCO	FQL	No analysis	
(86)	Case-control	Rural residence	JCO	FQL	No analysis	
(86)	Case-control	Species: C.jejuni	JCO	FQL	No analysis	
(44)	Case-control	Race: white vs other	NS	FQL	No analysis	
(90)	Cross-sectional	Metro vs suburban and rural areas	J	QL/MCL	No analysis	
(90)	Cross-sectional	*Campylobacter* species	JC	QL	No analysis	
(90)	Cross-sectional	*Campylobacter* species	JC	MCL	No analysis	
(44)	Case-control	Education: bachelor's degree or higher vs other	NS	FQL	p<0.01	N/A
(44)	Case-control	Residence: urban/suburban vs other	NS	FQL	p=0.02	N/A
(44)	Case-control	Household income: >60,000 vs lower	NS	FQL	p=0.02	N/A
(44)	Case-control	Sex: male vs other	NS	FQL	p=0.55	N/A
(99)	Cross-sectional	Age (years)	J	FQL	N/A	OR = 1.05 (0.99-1.1), p=0.0536
(78)	Case-control	Domestically acquired infection 1: student	NS	FQL	OR = 0.0 (0.0-0.7), p=0.01	N/A
(78)	Case-control	Employment status 2: student	NS	FQL	OR = 0.2 (0.0-0.7), p=0.02	N/A
(78)	Case-control	Living with a child under 5 years (versus not)	NS	FQL	OR = 0.3 (0.2-0.7), p=0.004	N/A
(78)	Case-control	Domestically acquired infection 2: living with child under 5 years	NS	FQL	OR = 0.4 (0.1-1.0), p=0.05	N/A
(98)	Case-control	Indigenous[e] acquired: summer (versus other seasons)	J	FQL	OR = 0.44 (0.32-0.60), p<0.001	OR = 0.46 (0.33-0.65), p<0.001
(98)	Case-control	Indigenous[e] acquired: school children	J	FQL	OR = 0.47 (0.22-1.03), p=0.05	N/A
(78)	Case-control	Gender [male vs other]	NS	FQL	OR = 0.9 (0.6-1.4), p=0.71	N/A

(99)	Cross-sectional	Sex (female)	J	FQL	OR = 0.92 (0.32-2.68), p=0.88	N/A
(98)	Case-control	Indigenous[e] acquired: retired individuals	J	FQL	OR = 1.32 (0.96-1.80), p=0.08	N/A
(90)	Cross-sectional	Age: over vs under 20	J	NS	OR = 1.4 (1.1-1.8)	N/A
(98)	Case-control	Indigenous[e] acquired: autumn (versus other seasons)	J	FQL	OR = 1.60 (1.21-2.12), p=0.0008	N/A
(98)	Case-control	Indigenous[e] acquired: winter (versus other seasons)	J	FQL	OR = 1.67 (1.24-2.26), p=0.0007	N/A
(98)	Case-control	Indigenous[e] acquired: semi-skilled manual workers	J	FQL	OR = 1.71 (0.96-3.04), p=0.06	N/A
(78)	Case-control	Employment status 1: employed	NS	FQL	OR = 1.8 (1.2-2.6), p=0.01	N/A
(90)	Cross-sectional	Race: Asian vs other	J	NS	OR = 2.3 (1.4-3.9)	N/A
(78)	Case-control	Age group 1/3: 18-44 vs <18 years	NS	FQL	OR = 2.8 (1.1-7.7), p=0.03	OR = 1.5 (0.5-4.0), p=0.47
(78)	Case-control	Age group 3: 65+ vs <18	NS	FQL	OR = 2.8 (1.1-8.1), p=0.04	OR = 2.0 (1.0-8.2), p=0.04
(99)	Cross-sectional	Season (winter)	J	FQL	OR = 3.27 (0.92-11.58), p=0.056	OR = 8.1 (0.9-72.7), p=0.0614
(78)	Case-control	Age group 2 = 45-64 vs <18	NS	FQL	OR = 4.3 (1.8-11.6), p=0.004	OR = 2.3 (0.9-6.2), p=0.09

[a]Study design was either specified by author or designated during data extraction
[b]*Campylobacter* species; NS=Not specified, J=*jejuni*, C=*coli*, F=*fetus*, L=*lari*, U=*upsaliensis*, O=other, [d]other, as specified in the text
[c]FQL=Fluoroquinolones, MCL=Macrolides, QL=Quinolones, TET=Tetracyclines
[e]The term 'Indigenous' is the term used in the source paper and can be considered synonymous with domestic acquisition (i.e., not obtained during travel)

*Per the scoping review protocol, data were only extracted if results compared resistant to susceptible. Data include the estimate of the measure of association from the model (OR = odds ratio), the 95% confidence interval in brackets, and the p-value.

Table 2.6. Key data extracted for food and food preparation factors identified in studies included in the scoping review for human infection with antimicrobial resistant *Campylobacter* species isolates compared to susceptible isolates, sorted by ascending univariable result.

Reference	Study Design[a]	Factor	Species[b]	AMR[c]	Univariable Result*	Multivariable Result*
(99)	Cross-sectional	Home prepared chicken	J	FQL	OR = 0.082 (0.0095-0.71), p=0.0095	N/A
(45)	Case-control	Handling of raw meat	J	FQL	OR = 0.14 (0.04-0.48), p=0.002	N/A
(98)	Case-control	Consumption of baby food	J	FQL	OR = 0.14 [0.03-0.74], p=0.0069	N/A
(45)	Case-control	Fresh chicken consumption	J	FQL	OR = 0.17 (0.06-0.45), p=0.0004	OR = 0.04 (0.004 to 0.39), p=0.005
(45)	Case-control	Beef (not cold cuts)	J	FQL	OR = 0.31 (0.13-0.73), p=0.008	N/A
(45)	Case-control	Sausages	J	FQL	OR = 0.32 (0.12-0.88), p=0.027	N/A
(78)	Case-control	Store raw chicken in fridge	NS	FQL	OR = 0.4 (0.3-0.7), p<0.001	N/A
(98)	Case-control	Indigenous[d] acquired: baby food	J	FQL	OR = 0.47 (0.20-1.10), p=0.08	N/A
(98)	Case-control	Indigenous[d] acquired: barbequed food	J	FQL	OR = 0.68 (0.44-1.06), p=0.08	N/A
(78)	Case-control	Domestically acquired infection 4: ate chicken in the UK	NS	FQL	OR = 0.7 (0.3-1.5), p=0.37	N/A

(78)	Case-control	Food history 1: eating away from home	NS	FQL	OR = 0.7 (0.4-1.0), p=0.07	N/A
(78)	Case-control	Food history 5: any unpasteurized milk	NS	FQL	OR = 0.9 (0.0-4.5), p=1.00	N/A
(78)	Case-control	Food history 3: any pork	NS	FQL	OR = 0.9 (0.6-1.3), p=0.05	N/A
(78)	Case-control	Food history 2: any chicken	NS	FQL	OR = 1.0 (0.5-2.0), p=0.91	N/A
(78)	Case-control	Domestically acquired infection 5: ate pre-cooked cold meats in the UK	NS	FQL	OR = 1.0 (0.5-2.1), p=0.91	N/A
(78)	Case-control	Handled raw chicken	NS	FQL	OR = 1.1(0.7-1.8), p=0.74	N/A
(98)	Case-control	Indigenous[d] acquired: eating in restaurants	J	FQL	OR = 1.25 (0.97-1.62), p=0.09	N/A
(98)	Case-control	Indigenous[d] acquired: fish and shellfish	J	FQL	OR = 1.29 (0.98-1.69), p=0.07	N/A
(98)	Case-control	Indigenous[d] acquired: organic vegetables	J	FQL	OR = 1.37 (0.95-1.96), p=0.09	N/A
(98)	Case-control	Indigenous[d] acquired: pate	J	FQL	OR = 1.44 (0.96-2.17), p=0.09	N/A
(78)	Case-control	Food history 4: any lamb or mutton	NS	FQL	OR = 1.5 (1.0-2.2), p=0.07	N/A
(98)	Case-control	Consumption of sausage	J	FQL	OR = 1.51 [1.00-2.29], p=0.0484	N/A

(98)	Case-control	Indigenous[d] acquired: cold meats (pre-cooked)	J	FQL	OR = 1.59 (1.16-22.21), p=0.004	OR = 2.13 (1.44-3.13), p<0.001
(98)	Case-control	Consumption of chicken	J	FQL	OR = 2.33 (1.29-4.22), p=0.0039	OR = 4.95 (2.12-11.56), p<0.001
(78)	Case-control	Travel-related infection 4: ate chicken abroad	NS	FQL	OR = 2.4 (0.6-9.7), p=0.17	N/A
(45)	Case-control	Fresh poultry other than chicken and turkey	J	FQL	OR = 2.40 (0.73-7.86), p=0.148	OR=19.10 (2.18-167.30) p=0.008
(78)	Case-control	Travel-related infection 5: ate eggs abroad	NS	FQL	OR = 2.6 (0.9-7.7), p=0.099	N/A

[a]Study design was either specified by author or designated during data extraction
[b]*Campylobacter* species; NS=Not specified, J=*jejuni*, C=*coli*, F=*fetus*, L=*lari*, U=*upsaliensis*, O=other,
[c]FQL=Fluoroquinolones, MCL=Macrolides, QL=Quinolones, TET=Tetracyclines
[d]The term 'Indigenous' is the term used in the source paper and can be considered synonymous with domestic acquisition (i.e., not obtained during travel)
*Per the scoping review protocol, data were only extracted if results compared resistant to susceptible. Data include the estimate of the measure of association from the model (OR = odds ratio), the 95% confidence interval in brackets, and the p-value.

Table 2.7. Key data extracted for travel factors identified in studies included in the scoping review for human infection with antimicrobial resistant *Campylobacter* species isolates compared to susceptible isolates, sorted by ascending univariable result.

Reference	Study Design[a]	Factor	Species[b]	AMR[c]	Univariable Result*	Multivariable Result*
(83)	Cross-sectional	Country of origin	J	MCL	No analysis	
(83)	Cross-sectional	Country of origin	J	FQL	No analysis	
(43)	Cohort	Domestically acquired infection vs travel acquired infection [two different drug classes explored]	NS	QL	No analysis	
(43)	Cohort	Domestically acquired infection vs travel acquired infection [two different drug classes explored]	NS	MCL	No analysis	
(77)	Prospective cohort	Susceptible vs norfloxacin resistant campylobacter jejuni in patients per travel destination	J	FQL	No analysis	
(78)	Case-control	Travel-related infection vs domestically acquired infection	NS	FQL	No analysis	
(79)	Cross-sectional	Travel-related vs domestic acquired infection	J	FQL	No analysis	
(84)	Cross-sectional	Travel to Spain (including the Canary Islands)	J	FQL	No analysis	
(84)	Cross-sectional	Travel to Thailand	J	FQL	No analysis	
(84)	Cross-sectional	Travel to India	J	FQL	No analysis	
(84)	Cross-sectional	Travel to China	J	FQL	No analysis	
(84)	Cross-sectional	Travel to Portugal	J	FQL	No analysis	
(86)	Case-Control	Foreign travel-related infection: symptoms started at least 2 days after the first day of travel outside the United States and Canada and within 3 days of returning [yes/no] Macro-region of infection source country: broken down by Latin America, Asia, Europe	JCO	FQL	No analysis	
(92)	Cross-sectional	Single destination international travel vs Multi/unknown destination international travel vs non-international travel	JO	QL	No analysis	
(92)	Cross-sectional	Multi/unknown destination international travel vs single destination international travel vs non-international travel	JO	MCL	No analysis	
(92)	Cross-sectional	Resistance based on travel to single destination	JO	QL	No analysis	
(92)	Cross-sectional	Macrolide resistant isolates based on single destination travel	JO	MCL	No analysis	

(94)	Cross-sectional	Travel associated human cases vs domestically acquired human cases in 2006 and 2007	J	MCL	No analysis	
(94)	Cross-sectional	Travel associated human cases vs domestically acquired human cases in 2006 and 2007	J	TET	No analysis	
(94)	Cross-sectional	Travel associated human cases vs domestically acquired human cases in 2006 and 2007	J	QL	No analysis	
(100)	Cross-sectional	Endemic vs travel-related *Campylobacter* infection	JO	FQL	No analysis	
(100)	Cross-sectional	Qualitative trends: tetracycline	JO	TET	No analysis	
(100)	Cross-sectional	Qualitative trends: macrolides	JO	MCL	No analysis	
(44)	Case-control	Foreign travel: yes vs no	NS	FQL	p<0.01	p<0.01
(93)	Case-control	Locally-acquired vs overseas-acquired by antibiotic	JO	FQL	p<0.05	N/A
(93)	Case-control	Locally-acquired vs overseas-acquired by antibiotic	J	TET	p<0.05	N/A
(93)	Case-control	Locally-acquired vs overseas-acquired by antibiotic	J	QL	p<0.05	N/A
(93)	Case-control	Locally-acquired vs overseas-acquired by antibiotic	J	MCL	p>0.05	N/A
(78)	Case-control	Travel-related infection 1: ill household contact	NS	FQL	OR = 0.2 (0.0-0.7), p=0.01	OR = 0.2 (0.0-0.6), p=0.009
(98)	Case-control	Africa (versus other countries)	J	FQL	OR = 0.24 (0.11-0.52), p=0.0001	OR = 0.11 (0.02-0.70), p=0.019; Interaction Term with consumption of mains water [OR = 9.17 (1.06-79.67), p=0.044]
(95)	Case-control	Travel within the United States outside of Minnesota	J	QL	OR = 0.3 (0.1-0.7), p=0.002	N/A
(98)	Case-control	France (versus other countries)	J	FQL	OR = 0.35 (0.16-0.74), p=0.0039	N/A
(98)	Case-control	Turkey (versus other countries)	J	FQL	OR = 0.41 (0.16-1.06), p=0.058	N/A

(78)	Case-control	Travel-related infection 2: Spain (versus other countries)	NS	FQL	OR =2.8 (0.9-9.7), p=0.07	N/A
(98)	Case-control	Portugal (versus other countries)	J	FQL	OR = 3.04 (1.04-8.89), p=0.0329	OR = 22.40 (4.36-114.99), p<0.001
(98)	Case-control	Cyprus (versus other countries)	J	FQL	OR = 3.53 (0.80-15.64), p=0.0764	OR = 11.74 (1.28-108.02), p=0.03
(95)	Case-control	Foreign travel: to Caribbean countries, South America, or Central America (not Mexico)	J	QL	OR = 4.5 (1.6-14.2), p<0.001	OR = 45.5 (9.7-214), p<0.001
(98)	Case-control	Travel to Spain (versus other countries)	J	FQL	OR = 4.79 (2.88-7.98), p<0.001	OR = 6.87 (3.52-13.38), p<0.001
(95)	Case-control	Foreign travel: to Mexico	J	QL	OR = 5.6 (3.1-12.6), p<0.001	OR = 26.0 (8.6-78.6), p<0.001
(95)	Case-control	Foreign travel: to Asia	J	QL	OR = 7.3 (2.8-21.7), p<0.001	OR = 40.7 (10.2-163), p<0.001
(90)	Cross-sectional	International travel	JC		OR = 12 (6.4-22.7)	N/A
(45)	Case-control	Travel abroad within the last 7 days	J	QL	OR = 12.12 (4.23-34.73), p<0.0001	OR = 16.81 (3.44-82.20), p=0.001]
(90)	Cross-sectional	International travel	J		OR = 12.5 (10.0-15.7)	N/A
(95)	Case-control	Foreign travel: to Spain	J	QL	OR = 14.0 (1.8-631), p=0.001	OR = 48.6 (4.1-570), p=0.002
(95)	Case-control	Foreign travel: Overall	J	QL	OR = 16.0 (7.8-38.8), p<0.001	N/A
(78)	Case-control	Travel abroad in last 7 days	NS	FQL	OR = 16.8 (9.7-29.6), p<0.001	OR = 24 (12.6-45.9), p<0.001

(99)	Cross-sectional	Foreign travel	J	FQL	OR = 35.7 (5.78-220.38), p<0.0001	OR = 33.4 (3.9-285.2), p=0.0013

[a]Study design was either specified by author or designated during data extraction
[b]*Campylobacter* Species; NS=Not specified, J=*jejuni*, C=*coli*, F=*fetus*, L=*lari*, U=*upsaliensis*, O=other, [d]other,as specified in the text
[c]FQL=Fluoroquinolones, MCL=Macrolides, QL=Quinolones, TET=Tetracyclines
*Per the scoping review protocol, data were only extracted if results compared resistant to susceptible. Data include the estimate of the measure of association from the model (OR = odds ratio), the 95% confidence interval in brackets, and the p-value.

Table 2.8. Key data extracted for factors related to underlying health conditions identified in studies included in the scoping review for human infection with antimicrobial resistant *Campylobacter* species isolates compared to susceptible isolates, sorted by ascending univariable result.

Reference	Study Design[a]	Factor	Species[b]	AMR[c]	Univariable Result*	Multivariable Result*
(91)	Cohort	Erythromycin use and HIV	JC	MCL	No analysis	
(85)	Cross-sectional	HIV	U	FQL	No analysis	
(88)	Case-control	HIV (n=16) vs non-HIV (n=5) [11 antibiotics tested]	J	QL	No analysis	
(88)	Case-control	HIV (n=16) vs non-HIV (n=5) [11 antibiotics tested]	J	FQL	No analysis	
(88)	Case-control	HIV (n=16) vs non-HIV (n=5) [11 antibiotics tested]	J	MCL	No analysis	
(88)	Case-control	HIV (n=16) vs non-HIV (n=5) [11 antibiotics tested]	J	TET	No analysis	
(44)	Case-control	Pre-existing medical condition: yes vs no	NS	FQL	p=0.55	N/A
(78)	Case-control	Diabetic (vs. not)	NS	FQL	OR = 0.3 (0.1-1.0), p=0.07	OR = 0.2 (0.0-0.9), p=0.031
(78)	Case-control	Antacid use in the previous month	NS	FQL	OR = 1.5 (0.9-2.4), p=0.099	N/A

[a]Study design was either specified by author or designated during data extraction
[b]*Campylobacter* Species; NS=Not specified, J=*jejuni*, C=*coli*, F=*fetus*, L=*lari*, U=*upsaliensis*, O=other
[c]FQL=Fluoroquinolones, MCL=Macrolides, QL=Quinolones, TET=Tetracyclines
*Per the scoping review protocol, data were only extracted if results compared resistant to susceptible. Data include the estimate of the measure of association from the model (OR = odds ratio), the 95% confidence interval in brackets, and the p-value.

Table 2.9. Key data extracted for water-related factors identified in studies included in the scoping review for human infection with antimicrobial resistant *Campylobacter* species isolates compared to susceptible isolates, sorted by ascending univariable result.

Reference	Study Design[a]	Factor	Species[b]	AMR[c]	Univariable Result*	Multivariable Result*
(45)	Case-control	Public water supply (Denmark)	J	FQL	OR = 0.17 (0.06-0.46), p=0.001	N/A
(98)	Case-control	Consumption of mains water while travelling	J	FQL	OR = 0.38 (0.23-0.62), p<0.001	OR = 0.24 (0.12-0.50), p<0.001; Interaction Term with travel to Africa [OR = 9.17 (1.06-79.67), p=0.044
(78)	Case-control	Food history 6: any tap water (UK)	NS	FQL	OR = 0.4 (0.3-0.7), p<0.001	N/A
(98)	Case-control	Indigenous[d] acquired: Private water supplies (UK)	J	FQL	OR = 0.45 (0.22-0.94), p=0.03	N/A
(98)	Case-control	Consumption of filtered jug water (UK)	J	FQL	OR = 0.56 (0.31-1.02), p=0.0539	N/A
(98)	Case-control	Swimming (UK)	J	FQL	OR = 1.47 (0.99-2.17), p=0.0531	N/A
(95)	Case-control	Drinking untreated water (US)	J	QL	OR = 2.0 (1.1-3.7), p=0.02	N/A
(95)	Case-control	Swimming (US)	J	QL	OR = 2.2 (1.3-3.7), p=0.002	N/A
(98)	Case-control	Consumption of bottled water (UK)	J	FQL	OR = 2.28 (1.30-4.00), p=0.0031	OR = 3.70 (1.69-8.10), p=0.001
(78)	Case-control	Food history 7: any still bottled water (UK)	NS	FQL	OR = 2.6 (1.7-4.0), p<0.001	N/A
(78)	Case-control	Food history 8: any sparkling bottled water (UK)	NS	FQL	OR = 2.9 (1.4-5.9), p=0.002	OR = 3.3 (1.5-7.2), p=0.002
(45)	Case-control	Swimming (pool, ocean, lake, or other place) (Denmark)	J	FQL	OR = 3.22 (1.48-7.00), p=0.003	OR = 5.01 (1.14-21.99), p=0.033)
(78)	Case-control	Domestically-acquired infection 3: drank sparkling bottled water in the UK	NS	FQL	OR = 3.4 (1.4-7.8), p=0.004	OR = 3.1 (1.3-7.2), p=0.011

(78)	Case-control	Travel-related infection 3: drank still bottled water abroad	NS	FQL	OR = 3.8 (0.8-18.4), p=0.05	OR = 5.2 (1.1-24.8), p=0.039

[a]Study design was either specified by author or designated during data extraction
[b]*Campylobacter* species; NS=Not specified, J=*jejuni*, C=*coli*, F=*fetus*, L=*lari*, U=*upsaliensis*, O=other
[c]FQL=Fluoroquinolones, MCL=Macrolides, QL=Quinolones, TET=Tetracyclines
[d]The term 'Indigenous' is the term used in the original paper and can be considered synonymous with domestic acquisition (i.e., not obtained during travel)
*Per the scoping review protocol, data were only extracted if results compared resistant to susceptible. Data include the estimate of the measure of association from the model (OR = odds ratio), the 95% confidence interval in brackets, and the p-value.

2.4 Discussion

2.4.1 Summary of evidence

This scoping review of 27 studies with factors related to human infection with antimicrobial resistant *Campylobacter* spp. provides insight into the available literature and the factors associated with these infections. While some themes of identified factors emerged with similarities between studies, this review primarily demonstrates the heterogeneity of available data and highlights the gaps that could benefit from further study. The factors and regions studied, the types of investigations, and the knowledge they contributed are broad and diverse. The populations included, data sources utilized, and analyses employed varied greatly. Travel was an important risk factor, and infections studied were commonly gastrointestinal infections with *Campylobacter jejuni* and were often evaluated using only a univariable analysis. Most of the studies were conducted in a small sample of high-income, westernized countries.

Risk factors

This review identified several important risk factors for antimicrobial resistant *Campylobacter* infections in humans. The foremost and most consistent of these was foreign travel (44, 45, 78, 90, 92, 93, 95, 99, 100). Care needs to be taken in interpreting this result as all travel studies only researched travel as a departure from a wealthy, westernized country, with highly inconsistent definitions of a comparator group. Travel is a complex variable that, in this context, is largely a proxy for a number of different, often unmeasured, factors including different water quality, differing food handling practices and microbial contamination, and potential exposure to different pathogens (32). Results from studies that compare foreign travel to domestic travel, or travel-acquired infections compared to domestic acquired infections, should likely be prioritized over those that only measured foreign travel in general or travel to a

specific country. Unfortunately, none of the studies that gathered this comparison provided a statistical analysis of their data.

The next most important category of factors identified are those related to prior antimicrobial use. Considering that antimicrobial use is a well-established risk factor for antimicrobial resistance in organisms including *Campylobacter* (1, 4), only seven of the included studies assessed prior antimicrobial use as a factor (45, 78, 80, 86, 89, 91, 95) and only five of the seven articles defined the interval for prior antimicrobial use as a month, or four weeks (45, 78, 80, 93, 95) and the start point of this interval included a month prior to: onset of illness (80, 95), onset of symptoms (45), infection (93), or stool sample (86). Prior antimicrobial use has been identified as a risk factor for other foodborne bacterial infections, such as *Salmonella* Heidelberg (102) and *Escherichia coli* (103). Consistency in assessing prior antimicrobial use is an important consideration in future research as the timing of prior use has been indicated to have an effect on resistant *E. coli* urinary tract infections (104) and may also apply to infections from resistant *Campylobacter*. Inappropriate antimicrobial prescribing and inadequate antimicrobial stewardship policies are known to exacerbate rates of antimicrobial resistant organisms (4), but only one included study measured an aspect of inappropriate antimicrobial stewardship, possession of non-prescribed antibiotics (86). Despite international calls for antimicrobial stewardship plans and policies (1, 4), no studies measured antimicrobial prescribing practices or stewardship and their relation to an antimicrobial resistant *Campylobacter* infection. It is also surprising that very few medical conditions requiring antimicrobial use were explored as comorbidities in the included studies. Only three articles looked at HIV and *Campylobacter,* but these articles only included count data (85, 87, 91). Other medical conditions frequently requiring antimicrobial use were not found in the included studies,

and may be a direction for future research, including: cystic fibrosis, urinary tract infections, and sexually transmitted diseases (1, 4). Lastly, reasons for prior antimicrobial use was not defined which may also provide important context to this factor, especially if it is a relapsed *Campylobacter* infection.

Animal contact, including contact with seemingly healthy pets, has been implicated as a risk factor for antimicrobial resistance in humans with methicillin-resistant *Staphylococcus aureaus* and antimicrobial resistant *Salmonella* spp., *Escherichia coli,* and enterococci (17, 105, 106). Antimicrobial resistant *Campylobacter* has been isolated from cats and dogs, and pet store puppies have been implicated in a large extensively drug-resistant *Campylobacter jejuni* outbreak in humans (107, 108). Animal contact was frequently measured as a risk factor in the included studies, but the results were mixed (45, 78, 95, 98, 99), suggesting that confounding or potentially interacting factors may be present.

Contaminated food, especially chicken meat, are known risk factors for a *Campylobacter* infection (70), but only four studies included a food-related factor in their analysis (45, 78, 98, 99). Due to antimicrobial use in agriculture, specifically broiler chicken farming, there is evidence of antimicrobial resistant and susceptible organisms travelling from farm to retail along the farm-to-fork pathway increasing the risk of antimicrobial resistant infections in humans (9, 109). Despite this, the results of the factors in this review, including those related to chicken consumption, are mixed. Some reasons for this could be regional differences in antimicrobial use in animals, regional differences in processing, and individual-level differences in food handling and safety. Additionally, some of the risk factors for resistant *Campylobacter* operate independently of the susceptibility of the strain, and factors that reduce the prevalence of *Campylobacter* spp. in general could have an impact on the prevalence of antimicrobial

resistance, yet these types of factors were not studied (110-113). Lastly, while only one study included a factor related to vegetables (98), antimicrobial use in plant agriculture and the use of manure from treated animals as a fertilizer for crops may be increasing the risk of antimicrobial resistant organisms in produce (4, 16, 114).

Many different iterations of water consumption and contact were explored in the included studies, but only four studies incorporated a water-related factor, the definitions of which were varied, and the results were mixed (45, 78, 95, 98). Water quality varies by region, which could be the main explanation for this finding. On the other hand, since all identified water factors examined fluoroquinolone or quinolone resistance in *Campylobacter*, and fluoroquinolone resistance in *Campylobacter* is known to be acquired through genetic mutations instead of through mobile genetic elements (MGE) potentially found in organisms in water (5, 115), this could be another reason why the results were mixed. Furthermore, if MGEs were the main source of resistance in *Campylobacter,* rather than through mutation, then we might expect more consistent results from contaminated water (5).

Antimicrobial resistance as a field of research

The multidisciplinary nature of antimicrobial resistance as a field of research and practice is undoubtedly necessary but made this review particularly difficult. The studies discussed factors on the individual patient level; however, antimicrobial resistance is a complex, population-level issue that needs to take into account the health of the environment, cleanliness of water, agriculture, inclusive of both food-crop and animal-husbandry practices, and the overall availability of antimicrobials and the prescribing nature of the physicians in the region (4, 16, 109). Foreign travel was one of the most commonly analyzed factors in the included studies and while there are a number of variables to consider within that factor that limit generalizability.

The more important dynamic to consider is that resistance does not recognize borders and more antimicrobial resistance surveillance in other countries, particularly travel destinations, is needed to curb the spread (32). Similarly, factors related to water were also common, but water quality levels vary greatly not only within countries but also between countries, further diminishing the generalizability of these findings. In addition to individual patient-level factors, population-level research on water quality, food-preparation, and antimicrobial stewardship would expand knowledge for risk-prevention strategies. An ecological study design, that uses a global One Health approach, would prove useful in this regard as it would capture large amounts of variation and in addition to containing the direct effects on the individual, indirect effects such as those mentioned above would also be captured (16, 116). Although there is always a trade-off, we would lose the ability to infer causality at the individual-level with ecological studies (116), therefore both levels of research are needed to understand the whole picture.

Study design considerations

Care needs to be taken when interpreting results, since not all study designs are created equal when it comes to determining factors for antimicrobial resistant infections (111-113, 116). Control group selection for case-control studies is key for determining whether the risk factor can be attributed to antimicrobial resistance and for controlling bias (111-113, 116). As previously stated, the most common study design of the included articles was a cross-sectional study design. While these studies are often used to measure the prevalence of *Campylobacter* and characteristics of a population at a given point in time, they represent statistical associations and provide weak evidence for causation because they do not have a strict control group (117). Cross-sectional studies also lack a time variable which are key to establishing causality and to dispute reverse causation (117). Results of cross-sectional studies provide an excellent starting

point for further exploration of risk factors but should be interpreted within the context of the year and location in which the study was done (117).

The second most-common study design of the included articles was case-control. In general, to identify the risk factors for infection with an antimicrobial resistant strain of *Campylobacter*, among people with *Campylobacter,* then the control or comparison group needs to be patients with antimicrobial susceptible *Campylobacter* (116). However, while this is the method used for this review as guided by the research question, this comparison group may not be appropriate for all of the factors identified in this study, especially prior antimicrobial use (113). If the comparison group is patients with *Campylobacter* infections that are susceptible to the antimicrobials of interest and that antimicrobial is used, then the results of that factor will be biased because that antimicrobial was an effective treatment, preventing that patient from being in the comparison group because their *Campylobacter* would be gone (116). Moving forward, the case-case-control or case-control-control study designs are becoming the preferred study design when examining factors related to antimicrobial resistant organisms since there are three groups: those with a resistant infection, those with a susceptible infection, and those who are healthy with at least one specimen to confirm, which allows researchers to better control for bias (111). While it falls beyond the scope of this review, controlling for time at risk is especially important since the longer the exposure to the risk the greater chance there could be of a negative outcome (116). For factors such as travel, there was no consideration of how long people were travelling for and similarly for antimicrobial use, there was no indication that length of treatment was controlled for in the analysis. A further consideration for future research would be to examine whether or not studies control for time at risk (116).

Lastly, the cohort study design provides a time aspect and the opportunity to measure multiple outcomes, but it is not well suited for the research question (116). Antimicrobial resistant *Campylobacter* infections, while increasingly common, are still relatively quite rare and cohort study designs typically do not handle rare outcomes well, often underestimating the odds ratios for the effect of a factor (116).

2.4.2 Limitations

Scoping reviews, by design, only capture research that is published and that are captured by the systematic search strategy, which means the factor list identified in this review is by no means exhaustive and begs the question about what factors exist for which published research is lacking or was outside the scope of this search. Additionally, a publishing bias prevents finding articles on null findings. Other limitations include a minor deviation from the protocol, which was clearly documented above during the review. As well, sixteen studies with data related to factors of interest could not be interpreted because they presented count data and did not complete an analysis appropriate to the research question, but some had enough data where an odds ratio could be calculated independently (44, 78, 79, 81-84, 86, 87, 89, 90, 92, 94, 96, 97, 100). Moreover, with only 27 included studies, often only one study presented data for a given factor. Due to the protocol decision to exclude non-English language articles during primary screening, there is a risk that pertinent factors were missed because they were published in other languages. Lastly, there is limited global generalizability because there were no studies from Africa and South America and 24 out of 27 studies were located in westernized, high-income countries.

2.5 Conclusions

This scoping review mapped current literature investigating factors related to antimicrobial resistant *Campylobacter* infections in humans. The heterogeneity of the results and articles provided a broad overview of the available factors while also illuminating areas for potential future research. These future research areas include studies examining time at risk and resistance, the effect of comorbidities that require antimicrobial use, and the recent effects of antimicrobial stewardship policies. Antimicrobial resistance is a global issue that would greatly benefit from an interdisciplinary, One Health research approach moving forward.

CHAPTER 3: MODELLING ANTIMICROBIAL RESISTANT *CAMPYLOBACTER* SPP. IN BROILER CHICKENS

Abstract

Campylobacter spp., commonly detected in poultry, are the third most common cause of foodborne illness in Canada. *Campylobacter* infections, while self-limiting and typically only requiring supportive care treatment, can be resistant to antimicrobials important to human health. With Canadian agri-food surveillance reporting recovery rates of 35% of *Campylobacter* in retail broiler chicken, it is important to determine the risk of exposure to antimicrobial resistant *Campylobacter* for the consumer. An integrated assessment model for antimicrobial resistance (iAM.AMR) has been developed in order to facilitate a holistic understanding of the potential for exposure of Canadians to resistant bacteria arising from agri-food production systems in Canada. The objectives of the iAM.AMR component developed here were to estimate the number of Canadians potentially exposed (NCPE) to *Campylobacter* spp. that are resistant to fluoroquinolones, macrolides, and tetracyclines from broiler chickens disseminated from farm to retail, to describe the role of factors related to fluoroquinolone, macrolide and tetracycline-resistant *Campylobacter* spp. in broiler chickens, and to identify associated knowledge and data gaps.

A comprehensive literature search synthesized the available, globally published literature on factors associated with antimicrobial resistance in *Campylobacter* spp. in broiler chickens. Data extraction consisted of characteristics of the study, the study population, and a description of and results for factor(s) investigated. Models for fluoro(quinolone), macrolide, and tetracycline resistance were built in Analytica using baseline surveillance data, odds ratios of factors, frequencies of factors, and consumer data. The search identified 7,344 de-duplicated

articles of which 15 articles were included in the qualitative synthesis after screening. Identified factors were allocated into the model at three stages of production: farm, abattoir, and retail. Factors included management practices, antimicrobial use on farm, chilling type at processing, and packaging type. Two scenarios were tested against a reference scenario to investigate:

1. How the Canadian context influenced human exposure to antimicrobial resistant *Campylobacter.*
2. How fluoro(quinolone) use in broiler chickens influenced human exposure to antimicrobial resistant *Campylobacter.*

This is the first application of an integrated assessment model for antimicrobial resistance in *Campylobacter* spp. from broiler chickens. This model framework can now be used for future understanding of the risk of exposure of Canadians from the broiler production chain. Overall, the model provided an overview of the influence of included factors on the estimated NCPE to antimicrobial resistant *Campylobacter* spp. from broiler chickens. There was a high degree of variability in the estimated NCPE in all scenarios and antimicrobial classes, illustrating the lack of robust data available in the literature. While estimated NCPE tended to increase with the number of factors included in the model, it is important to keep in mind that this model is not well suited to or intended to assess causal relationships. Two important assumptions inherent in the current model methodology are that modeled factors occur independent of each other and that they occur concurrently. These methodological issues limit interpretation of the model outputs as absolute values but the principle intent is to assess relative change when factors are varied and pathway outputs relative to each other. The model highlighted a number of key data gaps: the general sparsity of baseline surveillance data resistant *Campylobacter* spp. at chick placement, lack of Canadian-specific factor data, lack of available data about the prevalence of broiler

chicken production types, and a lack of data on potential factors at the transport, abattoir and retail nodes.

3.1 Background

Antimicrobial resistance, AMR, is a rapidly growing, complex global health threat that can impact severity and duration of illness, increase health care costs; it has the potential to exhaust all available treatment options (1, 4). Antimicrobial use is the predominant driver of AMR, and as such there are now resistance mechanisms for every known drug and class of antimicrobials (1, 4). To understand and address the threat and complexity of AMR, it is important to use a One Health approach taking into consideration the intersection of human, animal, and environmental health. With antimicrobials being used across multiple One Health sectors such as terrestrial livestock, aquaculture, crops, veterinary and human medicine, and with AMR occurring naturally in the environment, resistance genes and resistant bacteria can spread from agriculture to humans and vice-versa directly by contact, through the food chain, and through the environment (1, 4, 16) .

Surveillance data is key in quantifying, monitoring, and tracking AMR in addition to guiding policy and identifying areas for interventions (12-14, 16). The Public Health Agency of Canada has a national antimicrobial resistance and use surveillance program, the Canadian Antimicrobial Resistance Surveillance System (CARSS), launched in 2015 (13). CARSS incorporates data from a number of sector-specific programs including the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS), initiated in 2002, which conducts surveillance on foodborne antimicrobial resistance in organisms in the food chain (food animals, food, and humans) and antimicrobial use in animals (13, 18).

It is estimated that in Canada, one in every four human bacterial infections are already resistant to the first-choice antimicrobial treatment (4). Resistant bacteria from agricultural sources are propagated to humans through foodborne transmission such as contaminated meat

(4). Every year, 1 in 8 Canadians (about four million) are affected by a foodborne illness and of these, there are about 11,600 hospitalizations and 238 deaths (118). *Campylobacter*, commonly detected in poultry and poultry meat products (70), is the third most common cause of foodborne illness in Canada (118). *Campylobacter* spp. have varying levels of resistance to antimicrobials important to human health including macrolides, fluoroquinolones, and tetracyclines (5, 49). For 2018, CIPARS reported recovery rates of 35% for *Campylobacter* spp. from retail broiler chicken samples (53) with estimates of resistance to at least one antimicrobial of interest, to be about 54% in broilers and chicken products (119). Given the occurrence of *Campylobacter* infections and its common detection in chicken products, it is important to determine the risk of human infection with antimicrobial resistant *Campylobacter* spp. for the consumer.

To understand and quantify the risk of AMR in the food chain in Canada, an integrated assessment model for AMR, the iAM.AMR, has been developed (9, 68). Integrated assessment models, used for complex systems like climate change research, are a structured process for incorporating knowledge from various disciplines and sources into a single model producing holistic and integrated insights for decision-makers (68). The iAM.AMR has an overall goal to describe the relative contributions of particular types of AMR from the major Canadian livestock species (cattle, chicken, swine, and turkey) to understand the overall risk of exposure of Canadians to resistant bacteria arising from these agri-food production systems in Canada (120). The iAM.AMR project, to date, focuses on the following:

1. Bacteria:
    a. *Campylobacter* spp.
    b. *Enterococcus* spp.
    c. *Escherichia coli*

    d. *Salmonella* spp.

2. AMR to the following antimicrobial classes:
    a. Fluoro(quinolones)
    b. Macrolides
    c. Tetracyclines
    d. Third generation cephalosporins
3. Food animal hosts:
    a. beef cattle
    b. broiler chickens
    c. swine
    d. turkey

The iAM.AMR incorporates factors and data identified in the literature to modify the baseline prevalence of AMR in a bacterium-drug-commodity combination and propagates this probability as the agri-food animals move from the farm to abattoir to retail to human exposure (i.e., the farm-to-fork pathway), with the outcome of interest being the number of people exposed or the servings at risk for each of the above combinations and how each factor affects this value (120).

The objectives of this study were twofold. The primary objective was to estimate the number of Canadians potentially exposed, NCPE, to *Campylobacter* spp., that are resistant to fluoro(quinolones), macrolides, and tetracyclines, from broiler chickens as they move from farm to retail using an integrated assessment model. The secondary objective was to describe factors related to fluoroquinolone, macrolide and tetracycline-resistant *Campylobacter* spp. in broiler chickens and identify knowledge and data gaps.

3.2 Methods

3.2.1 Literature search

A comprehensive literature search approach was devised for the overall iAM.AMR to synthesize the available, globally published literature on factors associated with AMR in the identified bacterial species and agri-food hosts. The literature search was conducted by a research team composed of epidemiologists and veterinary epidemiologists with expertise in AMR, a research librarian, trained graduate students, and research assistants. For the iAM.AMR, a factor is defined as a practice, circumstance or fact that positively or negatively influences the occurrence of AMR in the farm-to-fork pathway. Factors are further delineated as modifiable, for example packaging type, or non-modifiable, for example farm location (120).

The following databases were searched: MEDLINE® in Ovid, AGRICOLA™ in ProQuest®, Centre for Agriculture and Bioscience abstracts in Web of Science, EMBASE® in Ovid, and Food Science and Technology Abstracts. The search strategy was developed in Ovid MEDLINE® (Appendix 3.1) and adapted for the remaining databases. References returned from the search were de-duplicated first in RefWorks (Ex Libris, Jerusalem, Isreal) and again after they were imported into Rayyan (Rayyan, Doha, Qatar) prior to primary and secondary screening. The search was initiated on April 11, 2019.

The primary screening strategy was pretested using 50 references and was designed to highlight any problems with the review process or software (120). Primary and secondary screening were completed by two independent reviewers. Primary screening reviewed the title and abstract of each reference and followed the decision tree for primary screening (Appendix 3.2). If consensus about inclusion status could not be reached between the two reviewers, a third reviewer was used to arbitrate (120). Secondary screening of the full text of the references was

performed using the secondary screening decision tree (Appendix 3.2). Any peer-reviewed, English language, analytic study, such as an observational or experimental study, that reported the effect of a modifiable factor that influences the occurrence of AMR was included. There were no limits placed on country or date of publication (120).

Data extraction was conducted using Microsoft Access (Microsoft, Redmond, Washington) and data were extracted by one reviewer. Data extracted were characteristics of the study, characteristics of the study population, and a description of and results for factor(s) investigated (120). Following the above stated definition of a factor, only modifiable factors, including their univariable, binary results, were extracted. If factors were assessed at multiple time-points, the measurement closest to human exposure was extracted. WebPlotDigitizer (Version 4.5, Ankit Rohatgi, Pacifica, California) was used to extract data from figures where numerical data were not presented. Factors related to multidrug resistance or factors that were influenced by the use of selective media were not extracted (16).

Data was exported from Microsoft Access into a Microsoft Excel (Microsoft, Redmond, Washington) for processing using R (R Core Team, Vienna, Austria), which calculated odds ratios, significance values, and meta-analysis results where applicable (120).

3.2.2 Determining factors for inclusion

A complete manual validation of extracted data against each full-text reference was performed. Isolation methods described in the full-text references were reviewed and references using selective media for isolation of antimicrobial resistant *Campylobacter* were excluded. References were reviewed to confirm that the factor was a modifiable practice or circumstance which influences the occurrence of AMR (120). Factors related to breed, location of farm, or age are non-modifiable factors and were excluded. Next it was confirmed that production stages were

clear for each factor. For example, if a farm made the decision to produce organic chicken, but the AMR levels were tested in isolates collected from retail chicken, then this factor was not included in the model. The factor also could not combine multiple production stages or commodities. For example, for the pathway combination examined in this study, layer chicken data could not be combined with broiler data, poultry data could not contain turkeys, and isolates from different stages of production could not be used unless they could be separated into each stage. Factors had to be well-characterized and have clear referent and comparator groups. The outcome of resistance also needed to be well-defined and for a specific antimicrobial. With the exception of common combinations of antimicrobials, such as sulfamethoxazole and trimethoprim, factors were excluded where general resistance to any drug or multidrug resistance was the outcome.

Following the manual validation, we determined factors for inclusion in the model. Experts from CIPARS with knowledge of the poultry industry and abattoir and retail foodborne AMR surveillance were consulted (Dr. Agnes Agunos, Dr. Anne Deckert, Allison Roberts, Public Health Agency of Canada, October-December 2021). The Chicken Farmers of Canada On-Farm Food Safety Program Manual (121) was reviewed for evidence of the applicability of specific factors to the Canadian broiler chicken industry (i.e., the factor is relevant or potentially relevant in Canada). Factors were reviewed for the possibility of combination via a meta-analysis. To be included in a meta-analysis, factors, whether between or within studies, needed to match on the following: same or similar factor definitions, the resistance outcomes were in the same antimicrobial class, and the unit of sampling, such as isolate, flock, or carcass, was the same. If appropriate, factors were then combined in a random effects meta-analysis per methods that exist within the iAM.AMR framework (120).

3.2.3 iAM.AMR Structure and inputs

The iAM.AMR is a quantitative, stochastic model developed in Analytica (Lumina Decision Systems, Los Gatos, California), with three main nodes to date: farm, abattoir, and retail. Model simulation employs Median Latin Hypercube sampling with 10,000 iterations to determine the uncertainty of the final outcome (66). An overview of the model and its structure can be found in Figure 3.1 and is explained in further detail below. For the pathway combination examined in this study, separate models were run in parallel for each antimicrobial class of interest: fluoro(quinolones), macrolides, and tetracyclines.

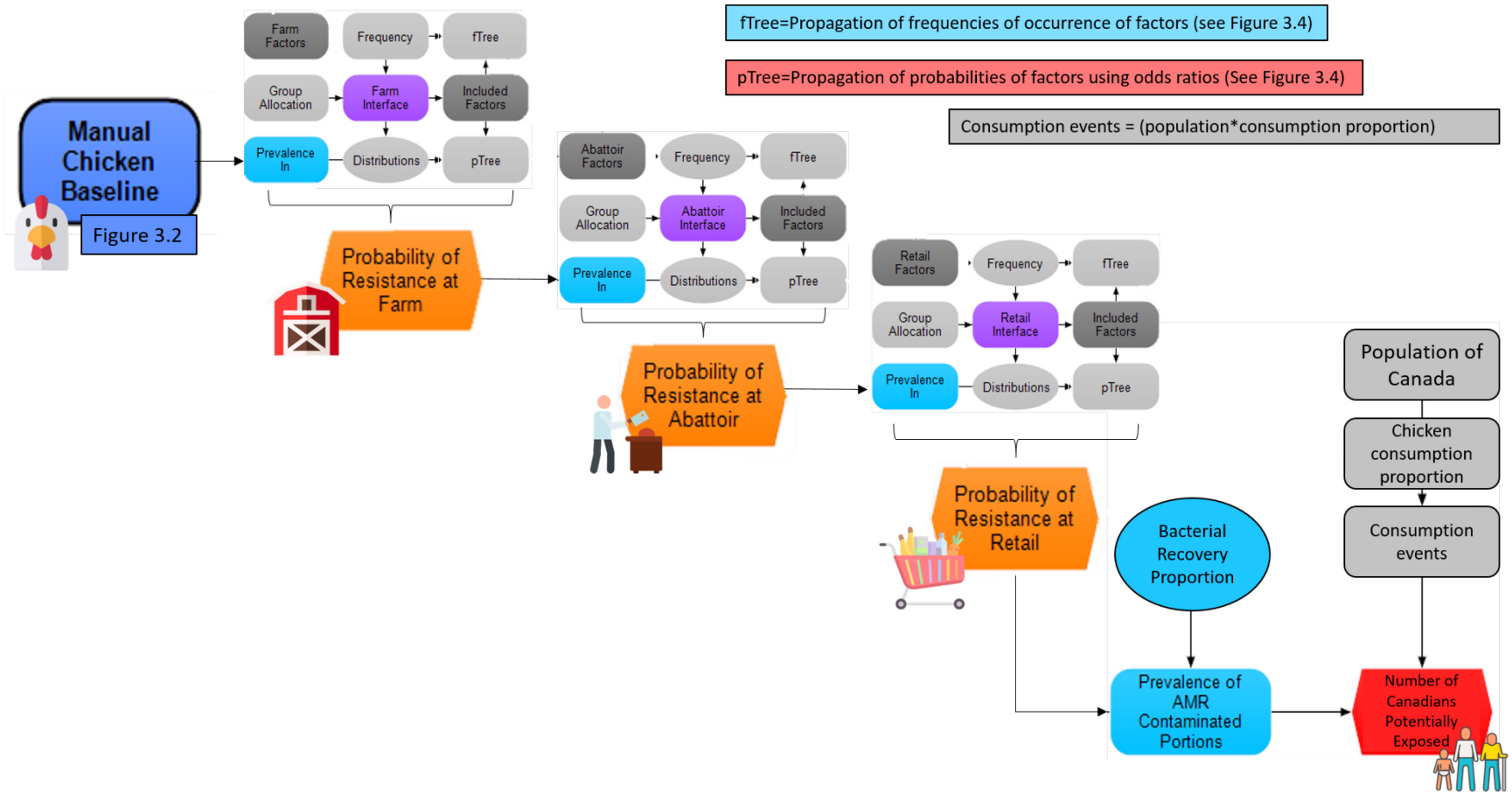


Figure 3.1. An overview of the integrated assessment model of antimicrobial resistant *Campylobacter* spp. in broiler chickens in Canada from baseline to number of Canadians exposed.

Table 3.1. Summary of parameters, descriptions, and the associated distributions and inputs for the integrated assessment model of antimicrobial resistant *Campylobacter* spp. in broiler chickens in Canada.

A	B	C	F	G
Parameter Type	**Description**	**Source**	**Uncertainty**	**Notes**
Baseline	Overall baseline amount of antimicrobial resistant *Campylobacter* in broiler chicken in Canada	(53, 122)	Pert distribution	See Figure 3.3 for more detail
	Baseline Max A	(122)	Beta distribution	
	Baseline Max B	(53)	Beta distribution	
	Selecting Baseline Max	(Dr. Agnes Agunos, Public Health Agency of Canada, email, November 2021)	Bernoulli distribution	
Odds Ratio	Flumequine use	(123)	Lognormal distribution	See Appendix 3.5
Odds Ratio	Tetracycline use	(124) (125)	Lognormal distribution	See Appendix 3.5
Odds Ratio	Fluoroquinolone (FQL) use	(123, 125-128)	Lognormal distribution	See Appendix 3.5
Odds Ratio	Ionophore use	(124)	Lognormal distribution	See Appendix 3.5
Odds Ratio	Avilamycin use	(124)	Lognormal distribution	See Appendix 3.5
Odds Ratio	Production type	(129-133)	Lognormal distribution	See Appendix 3.5
Odds Ratio	Tylosin use	(134)	Lognormal distribution	See Appendix 3.5

Odds Ratio	Meat chilling type	(135)	Lognormal distribution	See Appendix 3.5
Odds Ratio	Packaging type	(136)	Lognormal distribution	See Appendix 3.5
Frequency	Frequency of flumequine use	(53, 137)	Pert distribution	Used enrofloxacin as a proxy for F(QL) use, in water: Min=0% Mode=1% (2018 national proportion) Max=3% (Max reported proportion by region)
Frequency	Frequency of tetracycline use	(53, 137)	Pert distribution	In water, tetracycline or tetracycline-neomycin: Min=0% Mode=1% (2018 national proportion) Max=8% (Max reported proportion by region)
Frequency	Frequency of fluoroquinolone use	(53, 137)	Pert distribution	Used enrofloxacin as a proxy for F(QL) use, in water: Min=0% Mode=1% (2018 national proportion) Max=3% (Max reported proportion by region)
Frequency	Frequency of ionophore use	(53, 138)	Pert distribution	In feed: Min=0% Mode=70% (2018 national overall proportion) Max=100% (Max reported proportion by region)
Frequency	Frequency of avilamycin use	(53, 137)	Pert distribution	In feed: Min=0%

				Mode=15% (2018 national proportion) Max=63% (Max reported proportion by region)
Frequency	Frequency of tylosin use	(53, 137)	Pert distribution	In feed: Min=0% Mode=14% (2018 national proportion) Max=29% (Max reported proportion by region)
Frequency	Frequency of production types	(Dr. Agnes Agunos, Public Health Agency of Canada, email, February 2022)	Pert distribution	Min=15% non-conventional Mode=18% non-conventional Max=21% non-conventional
Frequency	Frequency of meat chilling type	(64)	Pert distribution	Min=0% Mode=1% Max=25%
Frequency	Frequency of packaging type	(139)	Pert distribution	See Appendix 3.6 Min=6% (lowest reported proportion) Mode=13% (overall proportion) Max=50% (estimated maximum)
Bacterial Recovery Proportion	Recovery proportion of campylobacter from broiler chicken at retail in Canada	(53)	Beta distribution	Used year 2015 201 *Campylobacter* samples 779 total samples
Consumption Proportion	The number of Canadians who reported consuming any chicken, not including deli meat, in the previous seven days	(140)	Pert distribution	Proportion: Min=84.0% (lower confidence interval) Mode=85.6% Max=87.3% (upper confidence interval)

Population	Population of Canada, total number of people potentially exposed	(141)	Not applicable	Used Q3 data 35.7 million

The main parameters of the *Campylobacter*-broiler chicken component of the iAM.AMR are summarized in Table 3.1. While the final outcome of the iAM.AMR is the estimated NCPE , in this case to fluoro(quinolone), tetracycline, or macrolide-resistant *Campylobacter* spp., inference can also be gained for how the individual factors affect the estimated NCPE for each AMR outcome of interest (66).

Ideally the baseline probability of antimicrobial resistant *Campylobacter* spp. in broiler chickens would have been sourced from CIPARS or other Canadian surveillance data and pulled from the earliest measured point of broiler chicken production currently included in the iAM.AMR - when the chicks are placed on the farm (53). However, the prevalence of *Campylobacter* spp. in broiler chickens at placement has never been assessed by CIPARS or any other surveillance program in Canada. The only available Canadian data on *Campylobacter* occurrence in chicks at placement were from an Ontario broiler farm study which ran from 2003 to 2004, and collected barn environment and bird-associated samples (122). Only two of 90 farms had any positive *Campylobacter* isolates at chick placement, a positive water sample from the drinker line and a positive chick liner swab (142), but only the water sample was available for susceptibility testing (122). While the relevant data are sparse they are derived from a large and representative sample. Due to the data sparsity, an ad hoc adjustment to the baseline was made to allow the model to run; the placement data were combined with CIPARS pre-harvest data and data from the literature and expert opinion were used, as summarized in Figure 3.2. This overall baseline probability was modelled using a Pert distribution that relied on a maximum from stacked input distributions using the data from Agunos et al., 2018 and CIPARS 2018, with the minimum and most likely values assumed to be zero (53, 122). A complete explanation of the methods of this baseline can be found in Appendix 3.4.

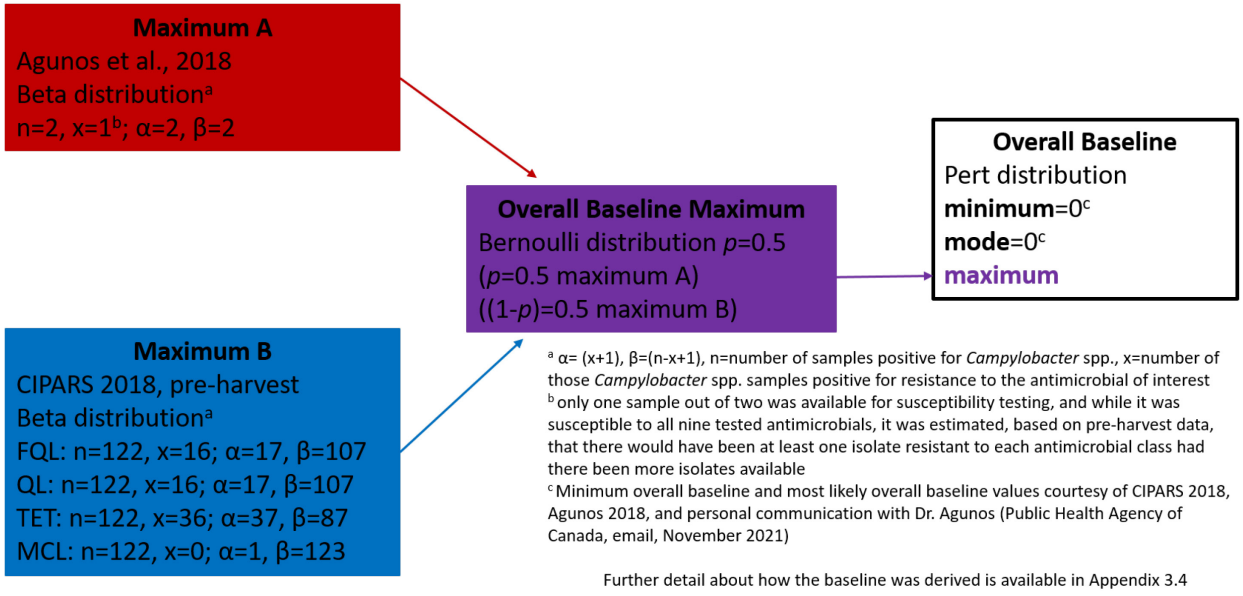


Figure 3.2. Description of the combined baseline of antimicrobial resistant *Campylobacter* spp. in broiler chickens in Canada used in the integrated assessment model.

Following manual validation, factors were included in their respective nodes using the odds ratios, standard errors, and p-values as calculated in R (66). Odds ratios were selected as model parameters for the following reasons: they are bound by 0 and can range to ∞, the estimated outcome is not altered by the order of the factors, and they are not linked to risk in the referent population, which increases their generalizability (66, 143). Uncertainty for each odds ratio was calculated by log transforming the odds ratios, producing a lognormal distribution, from which the standard error of the log odds ratio could be calculated. These were then converted back to the linear scale by exponentiating them (see Appendix 3.3) (66).

To modify the model so that it was applicable to the Canadian context, the frequency of occurrence of each factor in Canada was included. Frequencies were determined through literature or expert opinion and could range from 0, does not occur, to 1, always occurs, and was

represented by a probability distribution. If the frequency was unknown for Canada and could not be reasonably estimated from literature from a comparable region or country, a default value of 0.50 was used per iAM.AMR methodology (66). Frequencies of antimicrobial use in Canada were reported based on route of administration in the Canadian context as reported in Agunos et al., 2020 or Agunos et al., 2019 and summarized in Table 3.1 (137, 138).

To measure the NCPE to antimicrobial resistant *Campylobacter* spp. from broiler chickens through the food-chain, the probability from the final retail node was modified by three additional inputs: the frequency of *Campylobacter* spp. recovered from chicken samples at retail in Canada (53), the frequency of human consumption of chicken from the Canada Foodbook survey (140), and the population of Canada (66, 141). To calculate the frequency of *Campylobacter* spp. recovered from chicken samples at retail, the total number of *Campylobacter* spp. isolates recovered from retail chicken was divided by the total number of retail samples tested (66). Lastly, an estimate of the Canadian population was obtained from Statistics Canada (141); 2015 was used for consistency with the timing of collection of the Foodbook data.

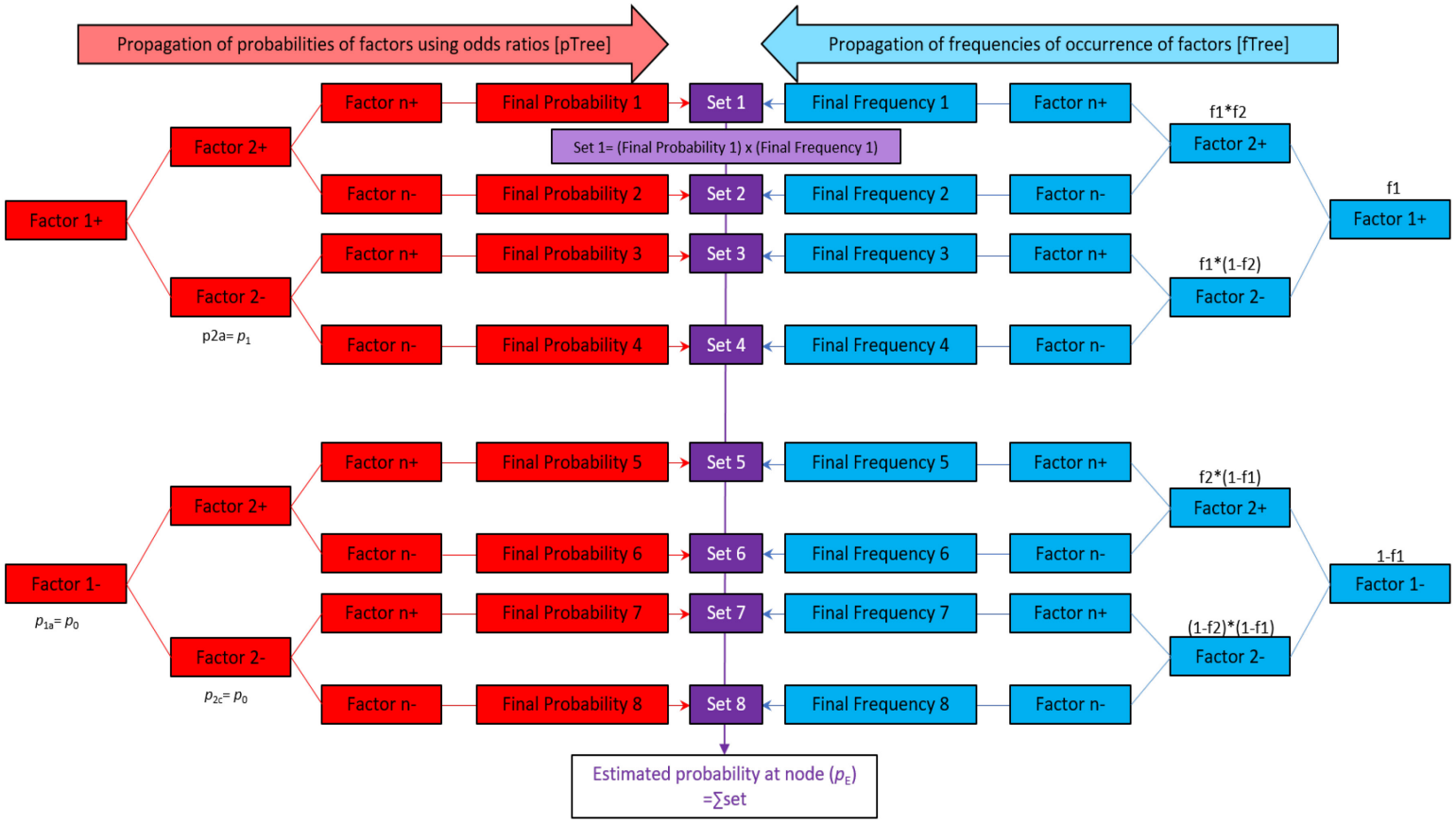
3.2.4 Propagation of probabilities in the iAM.AMR

To calculate the outcome, probabilities were propagated as they move from baseline through the three main nodes: farm, abattoir, and retail (66). A summary of how the probabilities of factors and their frequency of occurrence are propagated within a node can be found in Figure 3.3 and is further explained in Primeau, 2020 (66, 143). The outcome probability from a node becomes the starting probability for the next node in the pathway (66). Lastly, the NCPE were calculated using the simplified equation (1) below where $P(\mathrm{AC})_{\mathrm{RETAIL}}$ is the probability of antimicrobial resistant *Campylobacter* spp. at the retail node (see Table 3.1 for parameter

details). Foodbook data reflects a seven day recall period which translates to NCPE per seven days (140).

(1) NCPE = [$P(AC)_{RETAIL}$ x (2018 Retail recovery proportion of *Campylobacter* in chicken)] x [(2015 Population of Canada) x (2015 Proportion who consumed chicken)]

Determining which scenarios to run in the model were decided *post hoc* and depended on which factors were extracted from the literature. Since one of the objectives of this study was to model resistant *Campylobacter* spp. in Canada, one of the scenarios was set to be as close to the Canadian context as possible, pending available factors.



Node: An element within the model that represents a particular site within the system of interest (e.g., farm, abattoir or retail); **Factor**: A measured observation, such as antimicrobial use, different management systems, disinfectant use at slaughter plants and packaging at retail; **OR**: odds ratio; **Factor n+**: The measure of association (red) (e.g., presence of antimicrobial resistance) or frequency (blue) in the *presence* of the factor (e.g., presence of antimicrobial resistance); **Factor n-**: The measure of association (red) or frequency (blue) in the *absence* of the factor (e.g., the absence of antimicrobial use); p_O: The prevalence of antimicrobial resistance at the measured earliest site in the modelled system (e.g., broiler chicks at placement in the barn); p_E: Estimated probability at a node after adjustment of the baseline probability by the odds ratio and frequencies of occurrence of factors. Depending on the location of the node in the model, the estimated probability may become the baseline probability of resistance for the next node (e.g., the estimated probability from farm node becomes baseline for the abattoir node); **fn:** frequency of occurrence of factors; **f+**: frequency of factors occurrence (e.g., 30% of animals are exposed to antimicrobials); **f-**: frequency of factor non-occurrence (e.g., 70% of animals are not exposed to antimicrobials).

Figure 3.3. A diagram of the propagation of probabilities within a single node in the integrated assessment model of antimicrobial resistance (adapted from (66, 143)).

3.2.5 Model assumptions

Based on a number of data limitations such as regional gaps in surveillance data, inconsistencies among study sampling units, and the interest in resistance at the antimicrobial class level, the following model assumptions were made *a priori*:

1. AMR is consistent in *Campylobacter* isolates from across Canada.
2. Frequencies of the factors are consistent across Canada and factors measured outside of Canada are applicable to Canada if Canadian data do not exist.
3. *Campylobacter* isolates are spread uniformly across the surface of retail chicken and AMR is uniform within the colony forming units on a piece of chicken.
4. Different sampling units, e.g., isolate, flock, and farm, have a uniform weight on the outcome of the model.
5. Factors are independent and do not correlate or interact with each other.
6. Factors occur concurrently within a node.
7. Resistance is uniform within an antimicrobial class.

3.3 Results

3.3.1 Results of the literature search

The search conducted for the *Campylobacter*-broiler chicken component of the iAM.AMR identified 7,344 de-duplicated citations. Of these, 6,562 citations were excluded during primary screening and an additional 394 references were excluded during secondary screening (Figure 3.4). Of the 388 references that were included in data extraction, 29 contained AMR data for *Campylobacter* spp. in broiler chickens and an additional 14 references were further excluded for documented reasons (Figure 3.4). Overall, 15 references were included in the qualitative synthesis resulting in 13 factors.

3.3.2 Summary of factors

A summary of the included factors can be found in Table 3.1 and Table 3.2 (for a complete list of extracted data, see Appendix 3.3). The majority (11/13) of the included factors were applicable at the farm node and were predominantly antimicrobial use factors (9/11). The factors did not contain results uniformly across antimicrobial classes: 8/13 reported an effect associated with fluoroquinolone resistance, 7/13 reported an effect associated with quinolone resistance, while 5 and 4 reported an effect associated with macrolide and tetracycline resistance, respectively. As some studies only reported results for *Campylobacter coli, Campylobacter jejuni,* or unspeciated *Campylobacter*, the decision was made to aggregate data up to the *Campylobacter* spp. level. This resulted in 2/13 factors not qualifying for inclusion in the model because they could not be aggregated up to this level since the total number of farms that were positive for *Campylobacter* and the total that were positive for resistant *Campylobacter,* regardless of species, was not available. Due to the variety of types of production of broiler chickens in Canada such as organic, antibiotic free, free-range, or conventional, production type factors were combined into conventional management practices compared to unconventional management practices. Of the 15 studies included, the top countries represented were the United States (4/15) and the United Kingdom (3/15); there were 0 studies from Canada. Years of study ranged from 1994 to 2018 (Appendix 3.5).

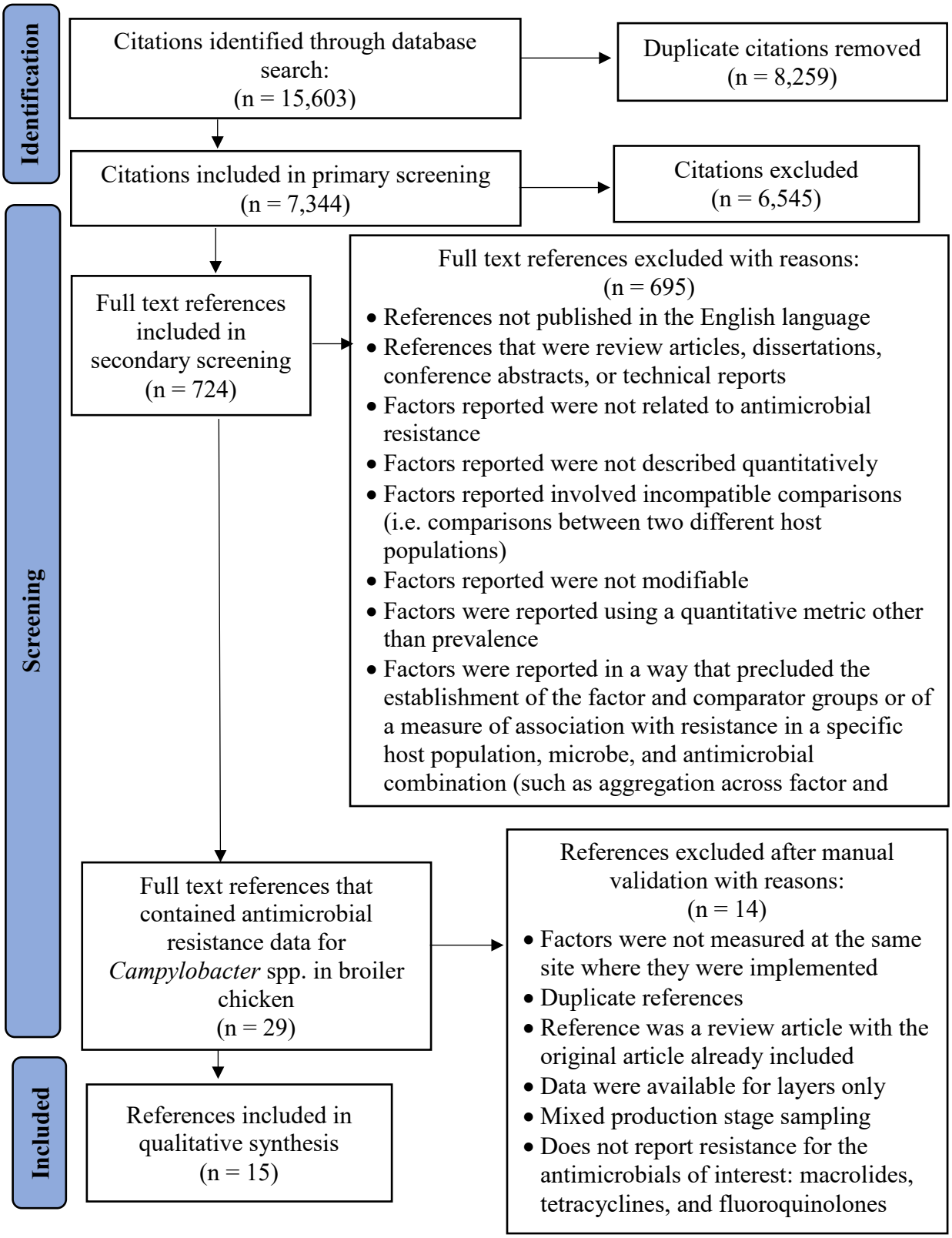


Figure 3.4. PRISMA flow diagram of the study selection process for the literature search to identify factors potentially associated with antimicrobial resistant *Campylobacter* spp. in broiler chickens in Canada (as of February 20, 2022).

3.3.3 Model scenarios and output

Integrated assessment models are not meant to be predictive. The purpose of the model is to better understand the relative contribution of the various factors to the probability of human exposure to antimicrobial resistant *Campylobacter* spp. Based on the availability of the extracted factors and consulting with veterinary public health experts with detailed industry knowledge (Dr. Agnes Agunos, Public Health Agency of Canada, personal communication, October-December 2021) two research questions were devised to explore the dynamics of the model and the contributions of the factors:

1. How does the Canadian context influence exposure to antimicrobial resistant *Campylobacter* spp.? (Table 3.2)

   Choosing from the available extracted factors, the Canadian context scenario included factors reflective of common practices in Canada. Meta-analysis factors were selected over single study factors. Duplicate factor types were included only if they did not have an overlap in resistance class data.

2. How does the inclusion of fluoro(quinolone) use influence exposure to antimicrobial resistant *Campylobacter* spp.? (Table 3.2)

   The fluoro(quinolone) use scenario was built onto the Canadian context scenario but included additional fluoroquinolone use factors for the fluoroquinolone- and quinolone-resistance models. While neither flumequine, nor any other quinolone, is known to be used in broilers in Canada, it was used as proxy in the model for potential quinolone use (Dr. Agnes Agunos, Public Health Agency of Canada, personal communication, October-December 2021). There were no fluoro(quinolone) or other antimicrobial use factors available for the macrolide-

or tetracycline-resistance models. As a result, these models were not run for this additional scenario.

Table 3.2. A summary of factors associated with antimicrobial resistant *Campylobacter* spp. in broiler chickens that were included in the integrated assessment models by antimicrobial class and scenario.

Scenario 1: No factors

Scenario 2: Factors which are common to the Canadian context

Scenario 3: Factors which are common to the Canadian context + **fluoroquinolones and quinolone use factors** (the factors for the MCL and TET models were the same as in scenario 2, so these scenarios were not run)

				All potential factors				Scenario 2				Scenario 3					
				Inclusion in the Antimicrobial Class Model													
Node	Factor	Factor Description	Unit[a]	FQL[b]	MCL[c]	QL[d]	TET[e]	FQL	MCL	QL	TET	FQL	MCL	QL	TET	Reference	MA[f]
Farm	Tylosin Use	Subtherapeutic vs therapeutic use	Animal													(134)	-[g]
Farm	Ionophore Use	Use vs no use	Flock													(124)	-
Farm	Avilamycin Use	Use vs no use	Flock													(124)	-
Farm	Flumequine Use	Use vs no use [Meta]	Isolate													(123)	WS[h]
Farm	Tetracycline Use	Use vs no use	Flock													(124)	-
Farm	Tetracycline Use	Use vs no use	Farm	*Not available for aggregation at unspeciated level*												(125)	-
Farm	FQL Use	Use vs no use [Meta]	Sample													(126, 127)	BS[i]
Farm	FQL Use	Use vs no use [Meta]	Isolate													(123, 128)	BS
Farm	FQL Use	Use vs no use	Farm	*Not available for aggregation at unspeciated level*												(125)	-
Farm	Production Type	Unconventional MP vs conventional MP [Meta]	Isolate													(129-132)	BS
Farm	Production Type	Unconventional MP vs conventional MP	Sample													(133)	-
Abattoir	Meat Chilling Type	Immersion chilling vs air chilling [Meta]	Carcass													(135)	WS
Retail	Packaging Type	Unpackaged vs pre-packaged	Carcass													(136)	-

[a]Sampling unit, [b]FQL=Fluoroquinolone model, [c]MCL=Macrolide model, [d]QL=Quinolone model, [e]TET=Tetracycline model, [f]MA=Meta-Analysis, [g]no meta-analysis, [h]WS=Within study meta-analysis, [i]BS=Between study meta-analysis

The results of the scenarios are summarized in Figures 3.5, 3.6, and 3.7 and were standardized to the 2015 Canadian population per 100,000. The probability densities of NCPE tended to be higher below 2,000 per 100,000 potentially exposed Canadians per 7 days and peaked at zero for all models, but particularly so for the "No Factor" model, with probability densities increasing for non-zero exposures for the Canadian and fluoroquinolone use models (Figure 3.5). There was a high amount of variability in the estimated NCPE in all scenarios and classes. Overall, the estimated NCPE increased as the number of factors included in the models increased. The estimated NCPEs were lowest in the "No Factor" models for all antimicrobials resistance classes, followed by the Canadian context models, and then fluoroquinolone use models (Figure 3.6). The largest change in estimated NCPE was for the macrolide resistance model, especially between the "No Factor" (median 101.71 per 100,000 Canadians per 7 days) and Canadian models (median 1,721.47 per 100,000 Canadians per 7 days, for brevity the "per 7 days" will be dropped from following results). Interestingly, the median estimated NCPE for the quinolone, macrolide, and tetracycline Canadian models were similar (ranging from 1,721.47 per 100,000 for the macrolide to 1,915.63 per 100,000 for the quinolone model). The Canadian fluoroquinolone model median was lower (965.12 per 100,000). There was more discrepancy between the median estimated NCPE among the AMR classes for the fluoroquinolone use models.

When investigating how the Canadian context influenced potential exposure to antimicrobial resistant *Campylobacter* spp., the Canadian model compared to the "No Factor" model, the median estimated NCPE increased compared to the average median and the "No Factor" model medians for all AMR classes (Figure 3.7). The lack of additional antimicrobial use factors precluded running this scenario for the macrolide- and tetracycline-resistance models.

When investigating the inclusion of fluoro(quinolone) use factors compared to the Canadian context for fluoroquinolone and quinolone resistance, the median estimated NCPE increased compared to the Canadian medians.

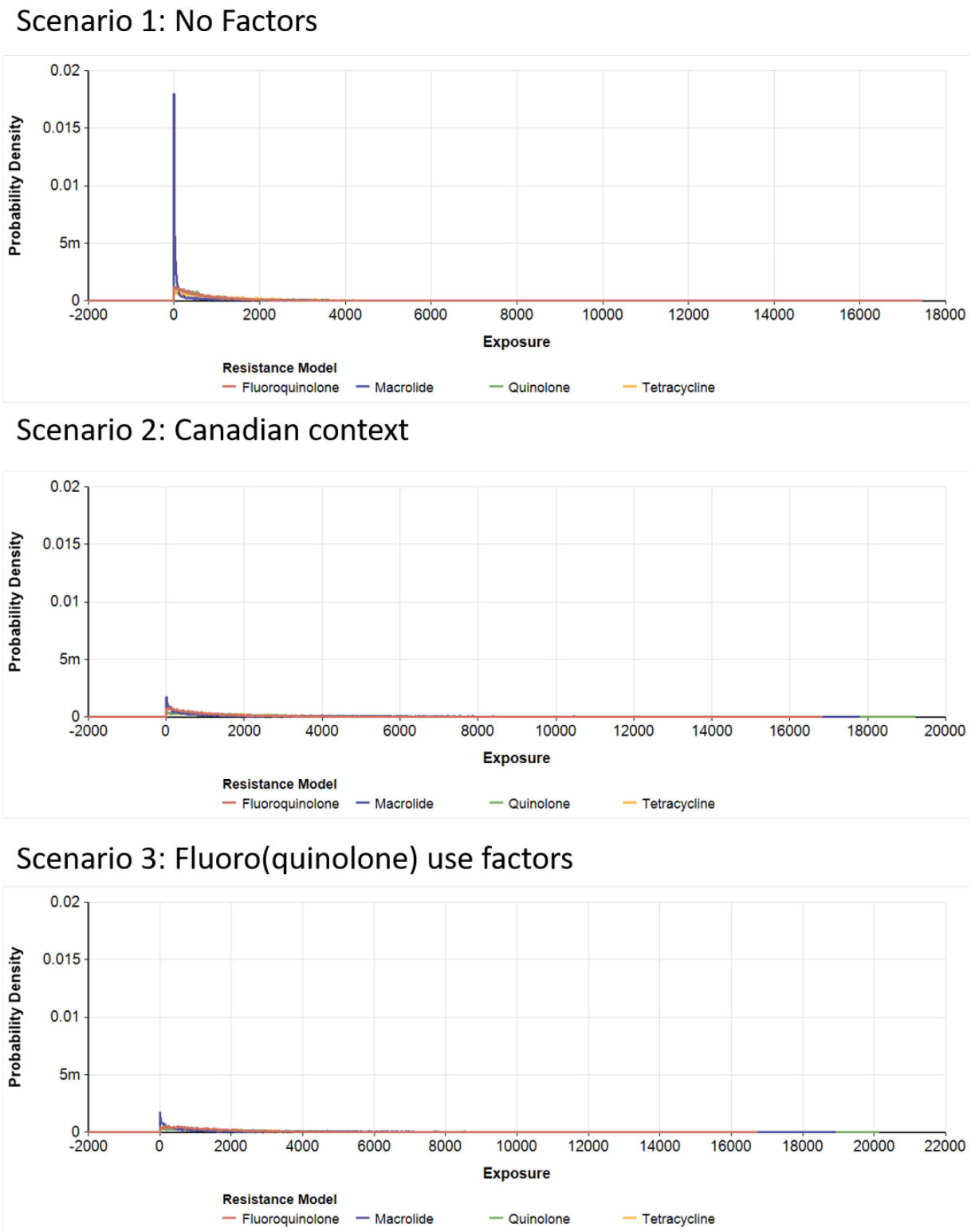
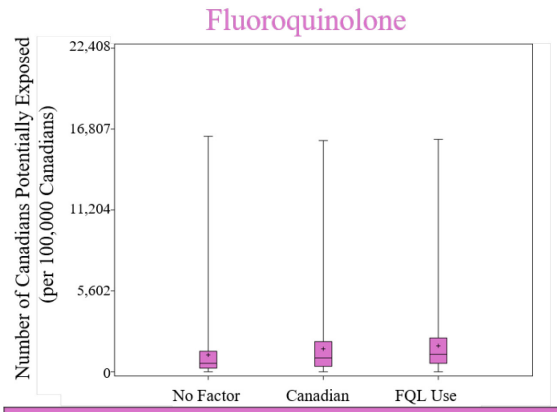
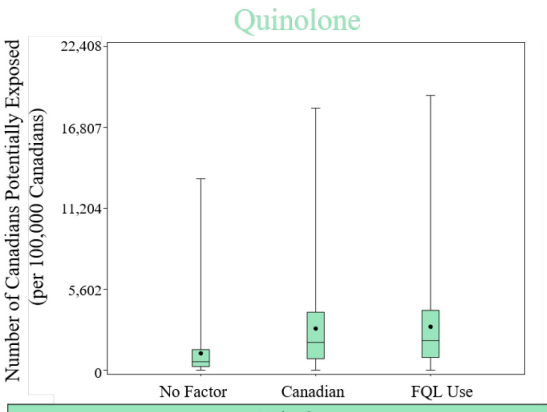


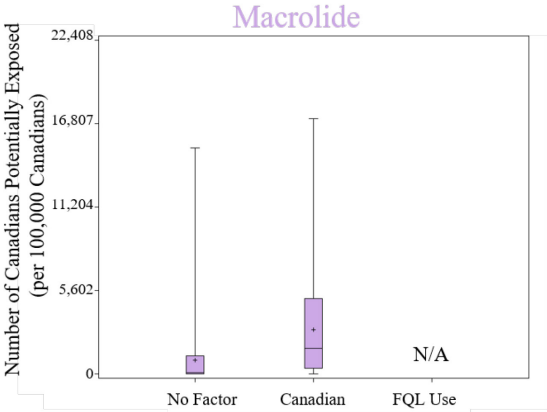
Figure 3.5. The simulated model probability distributions of the estimated number of Canadians potentially exposed (standardized per 100,000 population) to antimicrobial resistant *Campylobacter* spp. from broiler chickens in Canada by antimicrobial resistance class and model scenario.



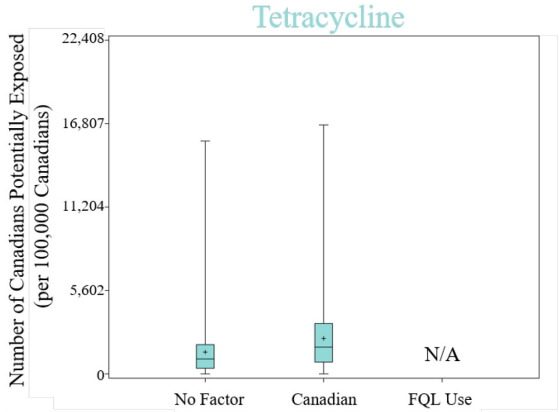
Fluoroquinolone			
	Scenario		
Statistics	No Factor	Canadian	FQL Use
Max	14,200.19	14,041.95	14,920.40
95th	4,550.37	5,506.68	5,724.34
75th	1,428.62	2,142.49	2,422.08
Median	**611.19**	**965.12**	**1,221.86**
25th	247.21	394.49	577.47
5th	41.77	67.89	123.29
Min	0.06	0.08	0.18
Mean	1,186.46	1,617.96	1,824.58
Std. Dev	1,554.10	1,821.10	1,837.98
Values are standardized per 100,000 Canadians			



Quinolone			
	Scenario		
Statistic	No Factor	Canadian	FQL Use
Max	15,600.60	19,066.81	18,792.79
95th	4,508.55	9,009.30	9,106.35
75th	1,409.92	3,942.17	4,069.13
Median	**613.05**	**1,915.63**	**2,052.65**
25th	245.87	792.71	889.60
5th	42.62	139.09	169.40
Min	0.03	0.11	0.32
Mean	1,175.05	2,857.30	2,966.77
Std. Dev	1,545.58	2,847.38	2,849.61
Values are standardized per 100,000 Canadians			



Macrolide			
	Scenario		
Statistics	No Factor	Canadian	FQL Use
Max	14,683.05	16,833.16	Not available for this resistance class model
95th	4,410.29	9,108.58	
75th	1,221.76	4,955.33	
Median	**101.71**	**1,721.47**	
25th	12.38	367.09	
5th	0.97	32.39	
Min	0.00	0.04	
Mean	936.19	2,960.59	
Std. Dev	1,630.17	3,081.18	
Values are standardized per 100,000 Canadians			



Tetracycline			
	Scenario		
Statistics	No Factor	Canadian	FQL Use
Max	16,623.20	16,989.77	Not available for this resistance class model
95th	4,487.81	6,739.11	
75th	1,990.10	3,439.00	
Median	**986.10**	**1,805.15**	
25th	409.39	769.69	
5th	71.96	140.90	
Min	0.08	0.10	
Mean	1,479.79	2,424.10	
Std. Dev	1,585.10	2,192.03	
Values are standardized per 100,000 Canadians			

Figure 3.6. Boxplot results from the simulated models of the estimated number of Canadians potentially exposed (standardized per 100,000 population) to antimicrobial resistant *Campylobacter* spp. from broiler chickens in Canada by antimicrobial resistance class and model scenario.

Legend
0 to 300
300 to 600
600 to 900
900 to 1,200
1,200 to 1,500
1,500 to 1,800
1,800 to 2,100
2,100 to 2,400

Antimicrobial Class	Scenario 1: No Factor	Scenario 2: Canadian	Scenario 3: FQL Use	CIPARS Retail Manual Comparison
Fluoroquinolone	611.19	965.12	1,221.86	3,006.26
Quinolone	613.05	1,915.63	2,052.65	3,006.26
Macrolide	101.71	1,721.47	Not available	3,006.26
Tetracycline	986.10	1,805.15	Not available	5,583.36

Values are standardized per 100,000 Canadians

Figure 3.7. Heat map of the model simulated median estimated number of Canadians potentially exposed (standardized per 100,000 population) to antimicrobial resistant *Campylobacter* spp. by antimicrobial resistance class and model scenario and colored due to their deviation from zero with the darker the red meaning more deviation compared to models using CIPARS 2018 retail surveillance data.

3.4 Discussion

3.4.1 Summary of evidence

This is the first application of an integrated assessment model approach to the risk of human exposure to antimicrobial resistant *Campylobacter* spp. in the broiler chicken farm-to-fork pathway. The model estimated the number of Canadians potentially exposed to *Campylobacter* spp., that are resistant to fluoro(quinolones), macrolides, and tetracyclines, from broiler chickens as they moved from farm to retail. The model also described factors related to fluoro(quinolone), macrolide and tetracycline-resistant *Campylobacter* spp. in broiler chicken and identified knowledge and data gaps.

The objectives of this research were to model scenarios for four antimicrobial classes: fluoroquinolones, quinolones, macrolides, and tetracyclines. However, based on the interest in fluoroquinolone resistance in Canada and the lack of factors throughout the farm-to-fork pathway for the macrolide- and tetracycline-resistance models for scenario 3, the interpretation and discussion of model results focused on the fluoroquinolone resistance model. Additionally,

based on the difference in factors available for inclusion between resistance models, the decision was made to focus on comparisons within resistance models rather than between resistance models.

Despite an industry initiated ban on the preventative use of category I antimicrobials, including fluoroquinolones, for broiler chickens in 2014 (54), the fluoroquinolone resistance model showed persistent resistance across all three scenarios. The 2018 CIPARS data on frequency of use indicated low to no use of fluoroquinolones in broiler chickens in Canada (53). Although fluoroquinolone use is allowed therapeutically, including for metaphylaxis, in chicken production, there are no approved products for poultry use in Canada, and any use is therefore off-label use requiring a valid veterinarian-client-patient relationship (Dr. Agnes Agunos, Public Health Agency of Canada, personal communication, October-December 2021) (57). Despite apparently limited fluroquinolone use the models suggested persistent potential for human exposure to fluoroquinolone-resistant *Campylobacter* from broiler chickens in Canada, consistent with CIPARS on-farm, abattoir and retail results (53). Given that fluoroquinolone resistance in *Campylobacter* tends to be the result of chromosomal mutation selected for by antimicrobial exposure, one might expect that based on the frequency data and timing of the ban that resistance levels would be low in the model, especially for the "No Factor" scenario, but this is not what the model suggested. If fluoroquinolone resistance in *Campylobacter* spp. came with a fitness burden to the organism, we would predict that resistance levels would fall with reduced fluoroquinolone use (62).

This direct relationship between use and levels of resistance was observed with ceftiofur resistance in *Salmonella* Heidelberg in broiler chickens, retail chicken, and human cases, where levels of resistance tended to correspond to use levels (144), yet this does not appear to be the

case with the model results. One explanation could be that there is more off-label use of fluoroquinolones in Canadian broiler chicken production than what CIPARS surveillance, which is based in absolute terms is a small number of sentinel flocks. The CIPARS on-farm program is representative of large scale broiler poultry production in Canada by virtue of inclusion in the program of the majority of Canadian veterinarians with a focus on poultry. It is estimated that participating veterinarians are responsible for 95% of the national flock. Because of this representation, and because veterinarians have the primary responsibility for antimicrobial sue the CIPARS on-farm poultry program is well situated to capture routine or standard use. However, in absolute terms data are collected on approximately 130-140 flock/cycles per year via a questionnaire representing about 0.4% of the national slaughter volume, with the farms the samples are collected from representing about 5% of the national flock (Dr. Agnes Agunos, Public Health Agency of Canada, personal communication, May 2021). Therefore, CIPARS is not necessarily well-suited for capturing situational use, such as a disease outbreak (53).

A further consideration is that fluoroquinolone resistance does not necessarily come with a fitness burden to *Campylobacter* spp., can therefore, potentially persist in the organism in the population even after the selective pressure of use has been removed (38). Combine this with the evidence that *Campylobacter* spp. can persist in the environment as well as being horizontally transferred by a number of vectors such as wild birds, contaminated water, flies, or mealworm beetles (26-28), and the ability for fluoroquinolone resistance to persist between broiler chicken flocks is plausible. This second explanation is supported by the literature where chicken colonization experiments have provided evidence that fluoroquinolone resistance does not carry a burden and can persist stably even after the selective pressure is removed (5, 38). The mechanisms of fluoroquinolone resistance in *Campylobacter* spp. could also be a factor in this

persistent resistance since this it arises from point mutation in the quinolone resistance-determining region of DNA gyrase A in conjunction with the CmeABC multi-drug efflux pump, rather than plasmid mediated resistance since mutations occur relatively often in *Campylobacter* (5, 38). This persisting resistant strain of *Campylobacter* can then be transferred between flocks at the barn, during transport, and during processing at the abattoir (26-28, 145). This could result in resistance levels that are relatively uniform between nodes and could explain why the three tested scenarios produced similar, overlapping results. Overall, these results suggest that there is persistent fluoroquinolone-resistant *Campylobacter* spp. in Canada in broiler chickens.

The quinolone resistance model displayed similar levels of persistence in the "No Factor" scenario, but unlike the fluoroquinolone resistance model, the quinolone resistance model displayed a potentially large increase for both the Canadian context scenario and again for the fluoro(quinolone) use scenario. The factor potentially driving this increase could be ionophore use, which was unique to the quinolone resistance model. Frequency of ionophore use, typically as a coccidiostat, in Canada ranged from 0%-100%, with the 2018 national overall proportion reported as 70% (53). It is possible that ionophore use could be interfering with the gut microbiota in broiler chickens making room for *Campylobacter* spp. colonization (146), although data to support this hypothesis is minimal and this model is not able to assess such a causal relationship. It may simply be that including the ionophore factor data are driving the simulated values in the quinolone resistance model.

The macrolide and tetracycline resistance models did not include any additional factors between the Canadian scenario and fluoroquinolone use scenario, which is why the fluoroquinolone use scenario was not available for these two resistance models. Ideally, there would be tetracycline and macrolide use scenarios for these respective models, but data were not

available. Interestingly, the only viable tetracycline use factor was linked only to fluoroquinolone resistance data for the fluoroquinolone resistance model. There is emerging epidemiological evidence that the fluoroquinolone and tetracycline resistance might be linked in *Campylobacter* spp. (147, 148); however, the lack of data precluded the ability to explore this relationship. As previously mentioned, the largest change in estimated NCPE occurred in the macrolide resistance model, although this was likely due to the sparsity of the baseline data (Agunos 2018) (122), or the sparsity of data leading to a zero-finding (CIPARS 2018 pre-harvest data) (53) for this antimicrobial class. The baseline, especially for macrolides, was heavily weighted towards zero probability of resistance, which is likely what is driving the low median NCPE for the 'No Factor' scenario. The median NCPE for the Canadian scenario seems relatively in line with the tetracycline and quinolone resistance models, but care needs to be taken when comparing between models as they contain different factors. Despite the lack of factors to build out these models to more fully reflect the Canadian context, the framework for these antimicrobial classes in broiler chickens has been established when future data are available.

3.4.2 Assessing model outputs

The outcomes of this model can be assessed by replacing the $P(\mathrm{AC})_{\mathrm{RETAIL}}$ in equation (1) below with 2018 CIPARS data from retail surveillance (Table 3.3) and calculating a crude estimate of NCPE and comparing these values to the estimated NCPE from the models. Median estimated NCPE using CIPARS 2018 retail surveillance data are presented in Table 3.3 and Figure 3.7 for comparison.

(1) NCPE = [$P(\mathrm{AC})_{\mathrm{RETAIL}}$ x (Retail recovery proportion of *Campylobacter* in chicken)] x [(Population of Canada) x (Proportion who consumed chicken)]

Table 3.3. CIPARS 2018 surveillance data of *Campylobacter* spp. in broiler chicken samples by resistance class at retail converted to probability of resistant *Campylobacter* at retail and the

median estimated number of Canadians potentially exposed, standardized per 100,000 using the CIPARS 2018 probability data in place of the probability of resistant *Campylobacter* at retail generated from the model.

	CIPARS 2018 Counts	CIPARS 2018 $P(AC)_{RETAIL}$	CIPARS 2018 Median Estimated NCPE (per 100,000 per 7 days)
Fluoroquinolones	14	0.1359	3,006.26
Quinolones	14	0.1359	3,006.26
Macrolides	14	0.1359	3,006.26
Tetracyclines	26	0.2524	5,583.36
Total number of *Campylobacter* spp. samples from chicken at retail	103		

Example simplified NCPE calculation: Fluoroquinolones

[0.1359 x 0.258] x [35,700,000 x 0.856] = [0.0350622] x [30,559,200] = 1,071,472.78

Standardized: (1,071,472.78 / 35,700,000) x 100,000 = 3,001.32 per 100,000*

*results may differ due to the use of distributions in the results in Table 3.3

Crude estimates using the CIPARS 2018 retail surveillance data appear to be higher than the model generated estimates for every resistance model. This suggests that the model is underestimating the probability of human exposure to antimicrobial resistance from *Campylobacter* spp. from broiler chickens. In contrast, when Primeau 2020 compared their model generated estimates for extended spectrum beta lactamase *E. coli* to estimates using CIPARS 2017 retail surveillance data, the model produced higher estimates than the surveillance estimates, suggesting an overestimation in this case (66). Overall, this comparison provides evidence that the model is not be accurately estimating the number of Canadians potentially exposed to antimicrobial resistant *Campylobacter* spp. from broiler chickens, but is functioning reasonably well at incorporating the factors extracted from the literature to generate an estimate.

3.4.3 Identifying important knowledge gaps

The high levels of variability in these models prevent a robust prediction of a conclusive end-point value of the estimated number of Canadians potentially exposed; however, meaningful information can still be garnered from the model. Not only does this model provide a framework of understanding AMR in *Campylobacter* spp. in broiler chickens and the potential risks to Canadians from the farm-to-fork pathway, but it also highlights important areas where data are lacking to focus future research, these include:

1. Limited baseline data, particularly recent data, for AMR in *Campylobacter* spp. from pre-placement broiler chickens. Despite robust sampling and data collection in Agunos et al., 2018, only two samples were positive for *Campylobacter*, and the one isolate tested for antimicrobial susceptibility showed no antimicrobial resistance. This sparseness of data was likely a reflection of true low occurrence rather than a lack of data or a methodological issue, and makes the need for corroborating evidence all the more necessary. This study only analyzed Ontario samples and representative Canadian baseline data continues to be data gap in this model. This gap limited the ability to populate the model with AMR prevalence in *Campylobacter* from chicks prior to any interventions, and future collection of these data over time could also monitor trends in AMR. In addition, if the baseline is truly sparse, methodological approaches to dealing with sparse data will have to be explored to improve model function.
2. A lack of data on factors for the Canadian broiler chicken context. While a strength of an integrated assessment model is its ability to incorporate and accommodate a broad range of data external to the context, Canadian-specific factor data is still preferred as broiler chicken production methods may vary between countries, which can affect the impact

that factors have on AMR (149). For example, while the Canadian poultry industry banned preventive fluoroquinolone use in broiler chickens in 2014, and the United States banned use in 2005, some of the world's top broiler chicken producers such as China, Poland, and Spain still use fluoroquinolones in broiler production (149). This combination of differing production methods and fluoroquinolone use practices makes it difficult to interpret the Canadian models to provide specific industry recommendations for interventions without more Canadian data.

3. Farm level factors such as the effect of biosecurity measures, animal husbandry practices, and flock-turnover practices were completely absent from identified factors and subsequently any of the models. These factors may provide evidence of risk or protective factors against AMR in broiler chickens, but without data, their measured effect is not known.
4. The proportion of broiler chickens in the Canadian market by production type was not readily available and as a result, the frequency of unconventional management practices compared to conventional management practices needed to be estimated based on expert opinion (Dr. Agnes Agunos, Public Health Agency of Canada, personal communication, October-January 2021). Production type, which can include conventional, free-range, organic, or antibiotic-free, is a high-level factor that can include a number of lower level, component factors such as antimicrobial use or biosecurity measures. Differing prevalence levels of *Campylobacter* spp. in broiler chickens have been indicated for different production types, with flock positivity being higher in organic and free-range birds, presumably due to environmental exposure (28, 58, 131). There also appears to be varying prevalence of the different *Campylobacter* species present by production type,

which is discussed further under Assumption 8 below (28, 58, 131). Additionally, while prevalence levels of *Campylobacter* spp. in general appear to be higher in these non-conventional production types, the levels of AMR tend to be lower, especially for organically raised birds (132, 150, 151). Conversely there is evidence that resistance levels may equalize in retail meat regardless of production type (150), which provides support for the need for surveillance along the entire farm-to-fork pathway and inclusion of non-conventional production types. Overall, the lack of information about the proportion of broiler chickens by production type in the retail marketplace in Canada is a major gap in understanding relative AMR.

5. There remains an important lack of data regarding transportation factors as birds are moved from farm to abattoir. Chapman et al., 2016 also identified this gap and it persists. Transportation factors such as crate type or bird collection type can affect the spread of antimicrobial resistant *Campylobacter* spp. from infected birds to uninfected birds (145).
6. While abattoir data regarding chilling type was included in the model, there are a number of processing steps absent from the included and available literature. Arguably, while each of these stages are modifiable and could influence the probability of consumer exposure to antimicrobial resistant *Campylobacter*, the lack of data prevented knowing where to best apply interventions to maximize the reduction of exposure or if an intervention at the abattoir stage would be effective in general.
7. In addition to gaps in abattoir data, there was also a notable lack of factors at the retail stage, as well as factors related to transportation between abattoir and retail. These data gaps have been well documented (145).

Some of the aforementioned gaps are consistent across multiple types of documented risk assessment models: transportation between abattoir and retail, portioning and packaging, rinse stages, and most abattoir stages, which supports the idea that data currently do not exist for these stages (63, 145). However, there are some gaps that are specific to this model, which suggests that the literature search did not capture all available factors or that the data were not in the form to be useful given the stated model inclusion and exclusion criteria. Furthermore, while the literature search focused on extracting data factors related to AMR, it is worthwhile to mention that any factor that reduces the prevalence of *Campylobacter* spp. in general could have an impact on the prevalence of AMR in *Campylobacter* spp. (110); however, because the overall iAM.AMR does not yet address these types of factors, they were not extracted and included in this model – this a key methodological evolution that will be necessary for the model to function optimally.

3.4.4 Addressing model assumptions

The *a priori* model assumptions come with potential trade-offs.

Assumption 1: AMR is consistent in Campylobacter isolates from across Canada.

It is very likely that resistance in *Campylobacter* varied region to region and while the CIPARS sampling regime is designed to be weighted by province according to the proportion of national flocks, it is a pooled and weighted sample and does not necessarily provide enough data to compare results between provinces. Additionally, part of the baseline is only derived from Ontario data, which further limits regional comparisons. These limitations in AMR surveillance data in Canada thereby prevented regional specific modelling and the results were instead applied at the national level (13, 53).

Assumption 2: Frequencies of the factors were consistent across Canada and that factors measured outside of Canada were applicable to Canada if Canadian data did not exist.

This assumption was out of necessity due to the data gaps discussed above. Some regional data existed for frequency of use of some antimicrobials by province in the CIPARS 2018 data (53), but this could not be implemented at the province level because we did not have provincial baseline data, nor was there consistent provincial data available for every factor included. The use of odds ratios to represent the factors were selected specifically because they are not linked to the referent population, allowing them to be applied to a different population than what they originated from (143).

Assumption 3: Campylobacter spp. was spread uniformly across the surface of retail chicken and AMR was uniform within the colony forming units on a piece of chicken.

While *Campylobacter* spp. will form colonies that may not be uniformly spread across a sampling area, it is pragmatic when modelling to assume uniformity both in colony distribution and their AMR at the cellular level. This comes with its own set of assumptions. Considering the mean generational time for *Campylobacter* spp. in broiler chickens was about 6.7 hours (152), there is a possibility that between sampling and culturing, the *Campylobacter* sampled is not the same generation as the one cultured. This also creates the possibility that the resistance profile could also change between sampling and susceptibility testing. This assumption is applicable to all *Campylobacter* spp. microbiology-based studies unless they are specifically designed to address this assumption and is not a unique weakness of this analysis.

Assumption 4: Different sampling units, e.g., isolate, flock, or farm, had a consistent impact on the outcome of the model.

To limit the potential for the ecological fallacy, the decision was made within the larger iAM.AMR modelling research group to abstain from combining sampling units such as isolate, flock, or farm within a meta-analysis. However, using multiple unit types within the model was acceptable since different nodes require different "ideal" units. For example, the ideal unit at farm node would be one bird compared to one carcass for the abattoir node and 100g of meat for the retail node. Out of modelling necessity, it was also assumed that resistance within these units was uniform, but it is important to note that the more a unit diverges from the ideal unit, the more uncertainty there is that the measured AMR likely applies to that ideal unit (Kayla Strong, University of Calgary, October-December 2021) (120).

Assumption 5: Factors are independent and do not correlate or interact with each other.

At the current stage of overall development and given the nature of the available factor data, the iAM.AMR makes the pragmatic assumption that factors are independent of each other; however, in many cases this may not be valid (120). This is especially true for the factors included at the farm node. As previously mentioned, production type is a high-level factor that can include lower-level component factors such as antimicrobial use. The lack of ability for this model to account for interaction or correlation between factors means that the relationships presented in the model results cannot be adjusted to include these dynamics. Ignoring statistical interactions in epidemiological models can have a large impact on the final estimates. For example, a survival analysis using a Cox regression model found that mis-specified interaction terms resulted in about a 9 fold bias in regression coefficients (153). Current knowledge gaps require this assumption because often these data from multivariable models are not available in the literature, particularly in a form that can be extracted and modeled using these methods. This presents an interesting and complex future direction for this research.

Assumption 6: Factors occur concurrently within a node.

Perhaps the most interesting assumption, and the area with the most potential for exploration in future research, is the assumption that factors occur concurrently within a node. In general, this model does not yet account for time. The only inclusion of time is in the separation of the farm, abattoir, and retail nodes. This model does not account for the order in which factors occur within the node, the length of exposure to factor, or how the lifespan of the broilers in comparison to other agri-food animals affects the overall time exposed and resulting risk estimates. This is less of a consideration for the abattoir and retail node of this specific model as there is only one factor in each, but it will become more important for nodes such as the farm node, or other models for other bacteria and commodities where more factor data are available. Determining the order and time in which these factors occur is no small challenge. This is another one reason why odds ratios were selected to represent factor data since the order in which they were included did not affect the end result (120, 143).

Assumption 7: Resistance is consistent within antimicrobial classes.

While the mechanism of resistance in *Campylobacter* spp. is more consistent within the fluoro(quinolone) antimicrobial class (2), the level of resistance among antimicrobials within a class can vary for macrolides and tetracyclines (2, 38). However, due to the objective of the research, antimicrobials were grouped into classes based on the World Health Organization ATC vet index (154). It is also unlikely that data would have been available to model specific drug resistance as evidenced by the data gaps in this study.

Assumption 8: Resistance and mechanisms behave uniformly across Campylobacter species (a post hoc assumption)

While data scarcity prompted the decision to aggregate *Campylobacter* data up to a species level, it is important to remember that the species do have differences. These include the overall predominance of *C. jejuni* in conventional broiler chickens, meat contamination, and human illness (27). There are also differences in AMR profiles between *C. jejuni* and *C. coli*. One study of small poultry flocks in Ontario, Canada, which included chicken, turkey, duck, and game bird flocks, found higher levels of tetracycline resistance in *C. jejuni* compared to *C. coli* (155). Conversely, Otto et al., found higher AMR in *C. coli* compared to *C. jejuni* from human infections in Saskatchewan, Canada (49). The lack of species-specific data precluded the ability to explore how these differences affected the estimated NCPE values.

3.4.5 Post-retail node considerations

This model investigated factors at the three main nodes of broiler chicken production: farm, abattoir, and retail. While it is beyond the scope of this research, it is important to consider the factors that occur post-retail. Quantitative microbial risk assessments of *Campylobacter* spp. in broiler chickens have identified that the factors with the greatest impact on human exposure are those at the post-retail consumer stage (63, 145). These include storage, cooking, cross-contamination events, and dose response dynamics. A sensitivity analysis by Dogan et al., suggested that the leading factor that prevented campylobacteriosis from broiler chicken in consumers was cooking temperature (63), a factor absent in the current model because general *Campylobacter* factors (vs antimicrobial-resistant *Campylobacter* factors) are not yet included. Two key next steps would be to:

1) Add a human exposure node after the retail node that would include factors related to human exposure to antimicrobial resistant *Campylobacter* spp. sourced from the literature.

2) Explore the human health outcomes of exposure to resistant versus susceptible *Campylobacter* spp.

3.4.6 In defense of integrated assessment models

A strength of integrated assessment models is their ability to integrate a variety of data types and sources from different regions to model and garner information about the relative contributions of different factors for complex phenomena, such as AMR in the food chain. They help to understand relative changes in exposure or impact when factors change between scenarios and to highlight possible intervention points (9, 66, 68, 120, 143). Other more mathematically robust modeling approaches are more suited to answering specific questions to describe and quantify AMR, such as quantitative microbial risk assessments (QMRA) and agent-based modelling (ABM). However, the intended purpose of integrated assessment models lies at a more holistic level, compared to these other approaches that aim to answer more specific questions (68).

Quantitative microbial risk assessments were first designed to model risk of chemical exposures, but have since been developed for use in drinking water and foodborne illness and AMR risk assessment, among other uses (156). The benefit of a QMRA over an integrated assessment model is that the end point value is often more reliable and accurate (156). Modelling AMR using a QMRA adds an additional layer of complexity to an already complex model, especially when assessing the dose-response aspect of a QMRA, since we not only need to consider the dose of antimicrobials to elicit resistance, or the time exposed to resistant genes to spread resistance, but also the dose needed to elicit illness in people (157). The downside of QMRAs is that they are complex, data intensive, and can take more resources to develop than integrated assessment models.

Agent-based modelling simulates actual transmission characteristics of pathogens and AMR through dynamic systems that aim to understand large-scale phenomena emerging from small-scale behavior (65). As such, this type of model would be very well suited to tackle the post-retail stage for AMR in the farm-to-fork pathway as it can simulate the micro factors such as food handling, storage, and personal antimicrobial use, to model the risk of AMR for the consumer. However, this model may not be well suited for modelling macro level factors at play in the broiler chicken industry (65). They are also very data, programming, and computer resource intensive, limiting the ability for development and implementation (65).

Despite these differences, all models will be subject to similar data gaps as described for this study. The benefit of choosing to model antimicrobial resistant *Campylobacter* spp. in broiler chickens using an integrated assessment model is the ability to include diverse data sources and have reduced complexity in terms of model construction and programming, and can provide the more efficient results that can be used for general policy considerations and decisions. To gain the best understanding of AMR in the food chain, results from this integrated assessment model should be used in conjunction with the more specific data from a QMRA and an ABM from future research. Furthermore, the antimicrobial resistant *Campylobacter*-broiler chicken pathway is a fundamental pathway in looking at AMR in the food chain and its development in the iAM.AMR is a key step towards constructing a more complete model linking across the other bacteria, host, and antimicrobial class scenarios.

3.4.7 Other limitations

Literature reviews, by design, only capture research that is published and that are captured by the designed search strategy, which means that the factors identified in this review are likely not exhaustive. The described reasons for exclusion contributed to this. Identifying the

missing factors was outside the scope of this project. Additionally, a publishing bias prevents finding articles on null findings. The literature review only included articles published in English, which means that there is a risk that pertinent factors were missed because they were published in other languages. It is also important to note that this model is likely not appropriate for measuring risk from backyard chicken producers, or small holder operations, especially those who choose to handle processing themselves since practices will vary greatly from conventional, large-scale production (158). Furthermore, this study only models one cycle through the production system and does not account for the potential cumulative effect of multiple cycles except for what is partially accounted for in the prevalence. The discussion of data gaps provides a thorough overview of the potential limitations of using this model to interpret farm level interventions to address AMR in *Campylobacter* in broiler chickens at this time. Filling these gaps with future research will improve the utility and application of the model.

3.5 Conclusions

This is the first application of an integrated assessment model for AMR in *Campylobacter* spp. from broiler chickens and provides a model framework for future understanding of the risk of exposure of Canadians. This study mapped current literature investigating factors related to antimicrobial resistant *Campylobacter* spp. in broiler chickens. The results of the integrated assessment model provided a broad overview of how the available factors influence antimicrobial resistant *Campylobacter* spp. from broiler chickens in Canada while also illuminating data gaps. These areas for future research include filling gaps in baseline surveillance data, a need for increased transparency about the prevalence of broiler chicken production types and extending the model past the retail node to include consumer practices and

human health outcomes.

CHAPTER 4: CONCLUSION

4.1 Overview of Study Results

Human infections with *Campylobacter* spp. are one of the top foodborne illnesses globally and antimicrobial resistance among *Campylobacter* spp. are a growing concern (26-29). With antimicrobial resistance potentially leading to increased duration of illness, increased length of hospital stays, rising economic costs and sociological impacts, it is important to identify factors that are potentially associated with resistance to help focus policy and interventions (4, 8). While there is conflicting evidence about whether a human infection with resistant *Campylobacter* spp. results in more adverse health outcomes than an infection with susceptible *Campylobacter* spp. (43, 45, 74), it is important to understand the factors and risk associated with *Campylobacter* to improve the overall understanding of resistance. Considering the greatest reservoir of *Campylobacter* spp. is poultry, including broiler chicken, it is key to understand the potential exposure to Canadians from broiler chicken and to investigate how different factors along the farm-to-fork pathway may affect the number of Canadians potentially exposed to antimicrobial resistant *Campylobacter* spp. from retail broiler chicken meat (26-29). One way to achieve this understanding of the factors affecting antimicrobial resistance in *Campylobacter* and the dissemination of antimicrobial resistant *Campylobacter* is through modeling. There are various approaches to modelling suited to answering specific questions and this thesis focused on developing the broiler chicken – antimicrobial resistant *Campylobacter* pathway from farm-to-fork as part of the overall iAM.AMR project (9, 66, 68). This thesis had to two main objectives.

Objective 1: To determine factors potentially associated with human infection with Campylobacter spp. that are resistant to fluoroquinolones, macrolides, or tetracyclines.

The scoping review identified 27 articles with factors related to human infection with antimicrobial resistant *Campylobacter* spp. The foremost and most consistent of these factors was foreign travel (44, 45, 78, 90, 92, 93, 95, 99, 100), often defined as departure from a wealthy, westernized country. Travel is a complex variable that can act as a proxy for many different unmeasured factors including different water quality, differing food handling practices, and potential exposure to different pathogens. Further work is warranted to better understand this relationship.

The next most important category of factors identified were those related to prior antimicrobial use, but only seven of the included studies involved a prior antimicrobial use factor (45, 78, 80, 86, 89, 91, 95). Only one study measured an aspect of inappropriate antimicrobial stewardship, possession of non-prescribed antibiotics (21). No studies measured antimicrobial prescribing practices or stewardship and their relation to an antimicrobial resistant *Campylobacter* spp. infection. These findings highlight the challenges with measuring and defining prior antimicrobial use in terms of clinical outcomes, such as how prior antimicrobial use is defined or what the timeframe for prior antimicrobial use were.

Animal contact (45, 78, 95, 98, 99), prior medical conditions (85, 87, 91), contaminated water (45, 78, 95, 98), and contaminated food (45, 78, 98, 99), especially poultry, were also indicated to potentially increase human risk of an infection with resistant *Campylobacter* spp. and are explored more in chapter two.

Objective 2: To develop an integrated assessment model component to evaluate the probability of human exposure to antimicrobial resistant Campylobacter spp. from broiler chicken in Canada resistant to fluoroquinolones, tetracyclines, or macrolides and identify knowledge and data gaps.

The data extraction from the literature search of the integrated assessment model of antimicrobial resistant *Campylobacter* spp. in broiler chicken in Canada identified 13 factors for inclusion, the majority of which were applicable at the farm node and were predominantly antimicrobial use factors. Three scenarios were modeled:

1) A baseline model with no factors included.
2) A scenario which included factors applicable to the Canadian context.
3) A scenario which included factors related to fluoro(quinolone) use within the Canadian context.

While the data from the 13 identified factors were not spread uniformly between the resistance models, overall, increasing the number of included factors tended to result in an increase in the estimated number of Canadians potentially exposed to resistant *Campylobacter* spp. from broiler chicken. Identified factors fell into one of the following categories: production type, antimicrobial use on farm, abattoir chilling type, or retail packaging type.

The probability density of the 10,000 iterations clustered heavily around zero Canadians potentially exposed which is likely a result of the baseline assumptions heavily favouring zero prevalence of antimicrobial resistant *Campylobacter* in broiler chicks, pre-placement. Results were standardized to the 2015 Canadian population per 100,000. However, this is not to say there is no probability of exposure as the median values range from 101.71 to 2,052.65 standardized per 100,000 estimated NCPE per 7 days and the maximum values, which range from 14,041.95 to 19,066.81 standardized per 100,000 estimated NCPE per 7 days suggest a much higher likelihood of exposure to *Campylobacter* spp. resistant to fluoro(quinolones), tetracyclines, or macrolides from broiler chicken in Canada. To put these values into context the estimated incidence of celiac disease in Canada is about 1,000 per 100,000 (159). In addition to likelihood

of exposure, we must also consider the consequences of a human infection with antimicrobial resistant *Campylobacter* spp. (156) which can include longer duration of illness, more severe illness, hospitalization, and, in rare instances, ReA, IBS, GBS, and MFS (4, 8, 26, 27, 29, 43, 45, 74). Overall it is important to consider both likelihood of exposure and its consequences to gain a more complete picture about the burden of a human infection with antimicrobial resistant *Campylobacter* spp. from broiler chicken in Canada.

Based on the interest in fluoroquinolone resistance in Canada and the lack of factors throughout the farm-to-fork pathway for different antimicrobial classes (specifically the lack of additional scenario 3 factors for the macrolide- and tetracycline-resistance models), the interpretation and discussion of model results focused on the fluoro(quinolone) resistance models. Additionally, based on the difference in factors available for inclusion between resistance models, the decision was made to focus on comparisons within resistance models rather than between resistance models. The main results of the fluoroquinolone use model were that despite a ban on the preventative use of fluoroquinolones for broiler chickens in 2014 (54), the fluoro(quinolone) resistance models showed persistent resistance across all three scenarios.

Although fluoroquinolone use is allowed therapeutically in chicken production, there are no approved products for poultry use in Canada and any use is therefore off-label use, including metaphylaxis, requires a valid veterinarian-client-patient relationship (Dr. Agnes Agunos, Public Health Agency of Canada, personal communication, October-December 2021). Furthermore, the CIPARS on-farm program can capture routine use but is not necessarily well-suited for capturing situational use (53). Despite low, and in some years no, detection of fluoroquinolone use, the reason for this persistence may be the result of the potential for added fitness from resistance mechanisms, horizontal transfer from environmental sources, and/or cross-over between flocks

during production stages (26-28, 38). The rate of mutations and the generation time contribute to the plasticity demonstrated in *Campylobacter* spp. Recall that fluoroquinolone resistance in *Campylobacter* occurs, in part, because of a point mutation in the quinolone resistance-determining region of DNA gyrase A, that affects the target for fluoroquinolones so that it is ineffective and is paired with an existing efflux pump, CmeABC, which works to decrease the amount of fluoroquinolone within the cell (5, 26-28, 38). This might also explain why fluoroquinolone resistance does not appear to come with a fitness burden on *Campylobacter* spp. (26-28, 38).

Other key results of this chapter included identifying top knowledge gaps such as: a sparseness of pre-placement baseline resistance data for broiler chicken in Canada, a lack of research on factors associated with transportation, abattoir node and retail node, and a lack of Canadian data for the proportion of conventionally raised broiler chicken. Two important assumptions of interest that require further development in the overall iAM.AMR model structure are that modeled factors occur independently of each other and that they also occur concurrently. The overall model architecture currently does not account for time or ordering of factors and there are not enough data to control and evaluate correlations or interactions between factors. The results of the integrated assessment model provided a broad overview of how the available factors influence antimicrobial resistant *Campylobacter* spp. from broiler chickens in Canada while also illuminating data gaps.

In addition to the above findings, both of chapter two and three highlighted areas for future research, some of which have also been echoed by others. These include an increased need for surveillance data for antimicrobial resistance, surveillance data that is truly integrated across sectors, regions, and livestock groups, and is standardized (13, 16). The scoping review

identified the following gaps and areas for future research such as: improved definitions of the travel and water quality factors, population-level research of the effects of the identified factors, and increased research of the effects of prior antimicrobial use on human infections with resistant *Campylobacter* spp. The integrated assessment model identified gaps consistent with findings from other *Campylobacter* models (63, 145) such as: baseline data for antimicrobial resistant *Campylobacter* in pre-placement broiler chickens, a lack of Canadian factor data, factors related to farm-level biosecurity measures, proportion of broiler chicken by production type in Canada, and a lack of research on factors at the abattoir and retail node.

4.2 Integrated Results

The overall objective of this thesis was to increase the understanding of the dissemination through the food chain and the factors affecting the occurrence of antimicrobial resistant *Campylobacter* spp. in broiler chicken and chicken meat in Canada, using an integrated assessment model approach as part of a broader integrated assessment model of antimicrobial resistance of the agri-food industry in Canada. Future directions of the research in general and specifically with respect to antimicrobial resistant *Campylobacter* and chickens, should go beyond exposure and incorporate consumer factors, infection, and the impact of antimicrobial resistance on the consequent human health outcomes. These consumer factors identified by using factor data from chapter two lay the groundwork for that direction of model development. However, neither chapters two and three capture transmission from broiler chicken to workers, an important area for future research (60, 160-162). Understanding the overall risk to humans from antimicrobial-resistant *Campylobacter* spp. would also need to include a consideration of the consequences of acquiring a resistant infection and so burden of illness would also need to be accounted for potentially through the use of a quantitative microbial risk assessment.

Specific future research directions and recommendations include implementing *Campylobacter* spp. testing for pre-placement broiler chicks in CIPARS data surveillance, determining the proportion of broiler chickens by production type in Canada, linking the results of the scoping review to that of the integrated assessment model, and exploring risk factors for workers along the production pathway.

4.3 Contextualizing the Current Research & Additional Future Research Considerations

While large knowledge gaps still exist for antimicrobial resistant *Campylobacter* spp. in Canada and around the globe, the gaps are slowly closing, and the pieces of the puzzle are slowly coming together. Broiler chicken, while the main reservoir, is not the only source of *Campylobacter* spp. Additional integrated assessment model components are currently being developed for *Campylobacter* in swine and beef cattle (9, 120). A quantitative microbial risk assessment of fluoroquinolone resistant *Campylobacter* spp. in broiler chicken is also under development as part of the overall suite of integrated assessment modelling and related risk modelling analysis initiatives (163). There has also been recently published data about trends in resistant *Campylobacter* spp. over time in Canada (49).

In addition to the future research directions suggested above, there are more areas that require future consideration which include: how climate change affects antimicrobial resistance (164), the impact of co-resistance with metals (6), how increased globalization and population movements as a result of conflict, climate change, (165) and large scale factors such as pandemics affect antimicrobial resistance (166). The effect of the COVID-19 on antimicrobial resistance levels has also yet to be quantified (167): whether that be a reduction due to increased public health measures or an increase due to higher levels of antimicrobial use from inappropriate prescribing and higher levels of hand sanitizer use. Next steps in regard to

antimicrobial surveillance also needs to include monitoring environmental prevalence and identifying sources of resistance.

It is important to reiterate that both studies restricted papers to English language publications and resulted in papers largely from westernized, high-income countries. Antimicrobial resistance and *Campylobacter* spp. infections are global concerns and to have a lack of data from a large proportion of the planet potentially exposes the research to important data gaps. If management practices are a factor in both *Campylobacter* spp. prevalence and the prevalence of resistance, it is likely that in cultures or regions where conventional management practices are not as common, that the results of this research may not apply.

4.4 Clinical and Public Health Implications

With the risk of an infection in humans with antimicrobial resistant *Campylobacter* spp. potentially increasing, it becomes ever more important to continue to push for antimicrobial stewardship policies to staunch and potentially reduce the growth and risk (38). Since antimicrobial resistance is an issue which intersects many policy areas, stewardship needs to be considered from a One Health perspective, and include agricultural sectors, in addition to the government and human health sectors (4, 13, 16, 24, 25). This includes evaluating ways in which we can reduce antimicrobial resistance at the farm such as finding alternatives to antimicrobial use, evaluating key interventions along the farm-to-fork pathway to reduce risk to the consumer, and adopting increased surveillance at the human level, specifically susceptibility testing of a patient when they present with a foodborne illness prior to prescribing antimicrobials which may exacerbate the issue.

4.5 Conclusions

This thesis contributes the first scoping review of factors potentially associated with human infections with antimicrobial resistant *Campylobacter* as well as the first integrated assessment model of antimicrobial resistant *Campylobacter* from broiler chicken in Canada. This model framework will serve to better understand the risks of foodborne transmission of antimicrobial resistance in *Campylobacter* to humans as future research adds to available data to do so. It also adds to the larger body of research that has identified gaps in data and knowledge related to antimicrobial resistant *Campylobacter* spp. Lastly this thesis suggests areas for future research to address these gaps and ways to add to the antimicrobial resistance field of research.

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APPENDIX INDEX

Appendix 1: No appendices for chapter 1

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Appendix 2.1: Scoping review protocol

The complete protocol for this scoping review, published in the Joanna Briggs Institute, includes a set of protocol appendices.

Appendix 2.2: All extracted data from scoping review

Tables with the complete set of extracted data from all included studies in the scoping review.

Appendix 2.2.1 Data extraction table 1

Which includes the following variables: Factor ID, paper reference, year of study, years the data were collected, study design, participant information collection method, study objective(s), method used for antimicrobial susceptibility testing, MIC interpretive criteria used, country of study population, the population sampled, and total sample size.

Appendix 2.2.2 Data extraction table 2

Which includes the following variables: Factor ID, paper reference, comparison group, sample size of the comparison group, method of identified participants, age details of the sample, proportion of females included, proportion of males included, proportion of unspecified gender included, and participant selection methods.

Appendix 2.2.3 Data extraction table 3

Which includes the following variables: Factor ID, paper reference, number of factors investigated, definition of factor, sample size of the exposed group, location of data, sub-

location of data, *Campylobacter* species, type of infection reported, type of resistance, type of analysis, type of result, result and measure of variation, statistical significance, any additional information about the factor, and additional notes about the paper.

Appendix 2.3: Data extraction form

Images of the data extraction form built in DistillerSR for the scoping review and includes two separate pages:

Data extraction form page 1 which contains questions 1-15

Data extraction form page 2 which contains questions 16-29

Appendix 3.1: Overall iAM.AMR Search Strategy

The search strategy used to search for articles to include in the overall iAM.AMR literature search, developed by the Health Library of Health Canada and the Public Health Agency.

Appendix 3.2: Data extraction forms for the iAM.AMR

Images of the data extraction forms built in Microsoft Access by the iAM.AMR research team which includes reference data extraction and factor data extraction. The image list includes:

Reference extraction
1-Basic Info
2-Study Info
3-Location
4-Auditing
5-Notes and Issues
Factor extraction form

Appendix 3.3: Decision trees for the iAM.AMR literature screening

Decision trees for primary and secondary screening of articles developed by and for the iAM.AMR literature search.

Appendix 3.4: Determining the baseline probability of antimicrobial resistant *Campylobacter*

An explanation of determining the baseline probability of antimicrobial resistant *Campylobacter* in broiler chickens

Appendix 3.5: Full Extracted Data Tables

Tables with the complete set of extracted data from all included studies in the literature review.

Appendix 3.5.1: Data Extraction Table 1

Which includes the following variables: paper reference, factor identifier, id number, study country, year of study, antimicrobial resistance, factor title, factor description.

Appendix 3.5.2: Data Extraction Table 2

Which includes the following variables: paper reference, id number, exposed group, referent group, odds ratio, standard error of the log odds ratio, *p* value, log odds ratio, meta-analysis id, meta-analysis antimicrobial class.

Appendix 3.5.3: Data Extraction Table 3

Which includes the following variables: paper reference, id number, meta-analysis type, host, *Campylobacter* species, allocation stage, observed stage, unit of sampling, result format, “A”, “B”, “C”, “D” (A-D described below).

	Count of AMR positive	Count of AMR negative

Exposed Group	A	B
Referent Group	C	D

Appendix 3.5.4: Data Extraction Table 4

Which includes the following variables: paper reference, id number, “P”, “Q”, “R”, “S”, total exposed, total referent (P-S described below).

	% of AMR positive	%of AMR negative
Exposed Group	P	Q
Referent Group	R	S

Appendix 3.6: FoodNet Canada Packaging Type Data

Data from FoodNet Canada about the overall proportion and counts of broiler chicken samples at retail that are packaged at counter and proportion and counts of broiler chicken samples at retail that are pre-packaged, from 2015 to 2020, data request made in December 2021

APPENDICES

APPENDIX 1

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APPENDIX 2.1

SCOPING REVIEW PROTOCOL

[In the following pages]

Factors associated with antimicrobial resistant *Campylobacter* spp. infections in humans: A scoping review protocol

Authors

Neustaedter C, Reid-Smith RJ, MacKinnon MC, Murphy C, Carson CA, Chapman B, Otto SJG (Final order and author list to be determined)

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Introduction

Campylobacter spp. is one of the leading causes of acute diarrheic illness in the world, accounting for 16% of foodborne illness globally (1) and 8.42% of foodborne illness in Canada (2). Infections are characterized by acute, watery progressing to bloody diarrhea and is often accompanied by abdominal pain, but vomiting is uncommon (3). *Campylobacter* has an incubation period of 2-4 days and most people recover within 2-5 days (4). An uncomplicated infection with *Campylobacter* typically only requires supportive care to avoid dehydration (4). Although uncommon, complications related to *Campylobacter* include but are not limited to bacteremia and increased risk of Guillain-Barré Syndrome (5).

Antimicrobials in the macrolide and quinolone family are commonly used in the treatment of *Campylobacter* infections and have been indicated to reduce duration of illness (6), providing that the infection is susceptible to these antimicrobials. Unfortunately, research indicates that *Campylobacter* has displayed resistance to macrolides, quinolones, and tetracyclines (7). Antimicrobial resistance is commonly defined as the ability of a microorganism to stop an antimicrobial from working against it, rendering standard treatments ineffective (8). Patients with a resistant strain of *Campylobacter* have an increased risk of an adverse health event such as invasive illness or death (9) and may have a higher rate of hospitalization than a susceptible infection (9). Patients with a resistant strain of *Campylobacter* may also experience a longer duration of illness (9).

The purpose of this scoping review is to determine what available published literature exists globally on factors associated with a human infection with antimicrobial resistant *Campylobacter* species. More specifically, factors associated with a human infection with a *Campylobacter* strain that is resistant to the antimicrobials: macrolides; tetracyclines; and/or quinolones, will be investigated. This scoping review will follow the Joanna Briggs Institute Reviewer's Manual framework for scoping reviews which defines the objectives, methods and reporting of the review to facilitate a transparent review process (10).

The term antimicrobial resistance (AMR) used in this review will refer to the ability of microorganisms, such as bacteria, fungi, or viruses, to withstand, to varying extents, the effects of an antimicrobial to which they were formerly susceptible (11). The search will not be limited by specific *Campylobacter* species, and resistance must be determined by recognized laboratory antimicrobial susceptibility testing methods. Factors will be assessed during the screening process using the intentionally broad definition of a practice or circumstance that positively or negatively influences the occurrence of AMR (12). This definition does not consider the concept of causality; we consider any relationship between an exposure and outcome as a factor, whether or not a causal pathway is present (12).

A preliminary search for existing reviews and relevant research was completed on January 21, 2020 in Ovid Medline®, Cochrane Library, Joanna Briggs Institute Systematic Review Registry, and Google Scholar. No scoping or systematic reviews were found but there were indications that relevant research exists. The objective of this review will be to gather existing research on risk factors for a human infected with an antimicrobial resistant *Campylobacter* species and characterize the body of evidence thereby establishing the array of risk factors in addition to exploring the variability between the studies.

Inclusion Criteria

Types of Participants

Any study that evaluates humans of any age with a *Campylobacter* infection (confirmed by recognized laboratory methods) will be included. Non-human research, studies that evaluate infections other than *Campylobacter*, studies that evaluate colonization instead of infection, and studies that fail to confirm a *Campylobacter* infection by culture will be excluded.

Concept

Studies must evaluate the exposure of interest which are factors involved with a human infection with a resistant *Campylobacter* strain, for example, known risk factors of age, recent travel, pre-existing medical conditions, but the search won't be limited to those mentioned. Studies which do not evaluate factors related to a human infection will be excluded. The comparator group will be appropriate to the study design. For example, when applicable, the comparator group for case-control studies will be infections with *Campylobacter* that are susceptible to the antimicrobials of interest. Our outcome of interest are studies evaluating resistance to our antimicrobials of interest: macrolides, tetracyclines, and quinolones. Resistance must be determined by recognized laboratory antimicrobial susceptibility testing methods.

Context

There were no limits applied to language, geographical location, *Campylobacter* species, and date published. Non-English articles will be identified and excluded during primary screening.

Types of Studies

The review will include any analytic study, including theses and dissertations. Study designs that will be excluded from the review are: review articles, commentary, opinion pieces, editorials, newspaper articles, books, book chapters, and conference proceedings.

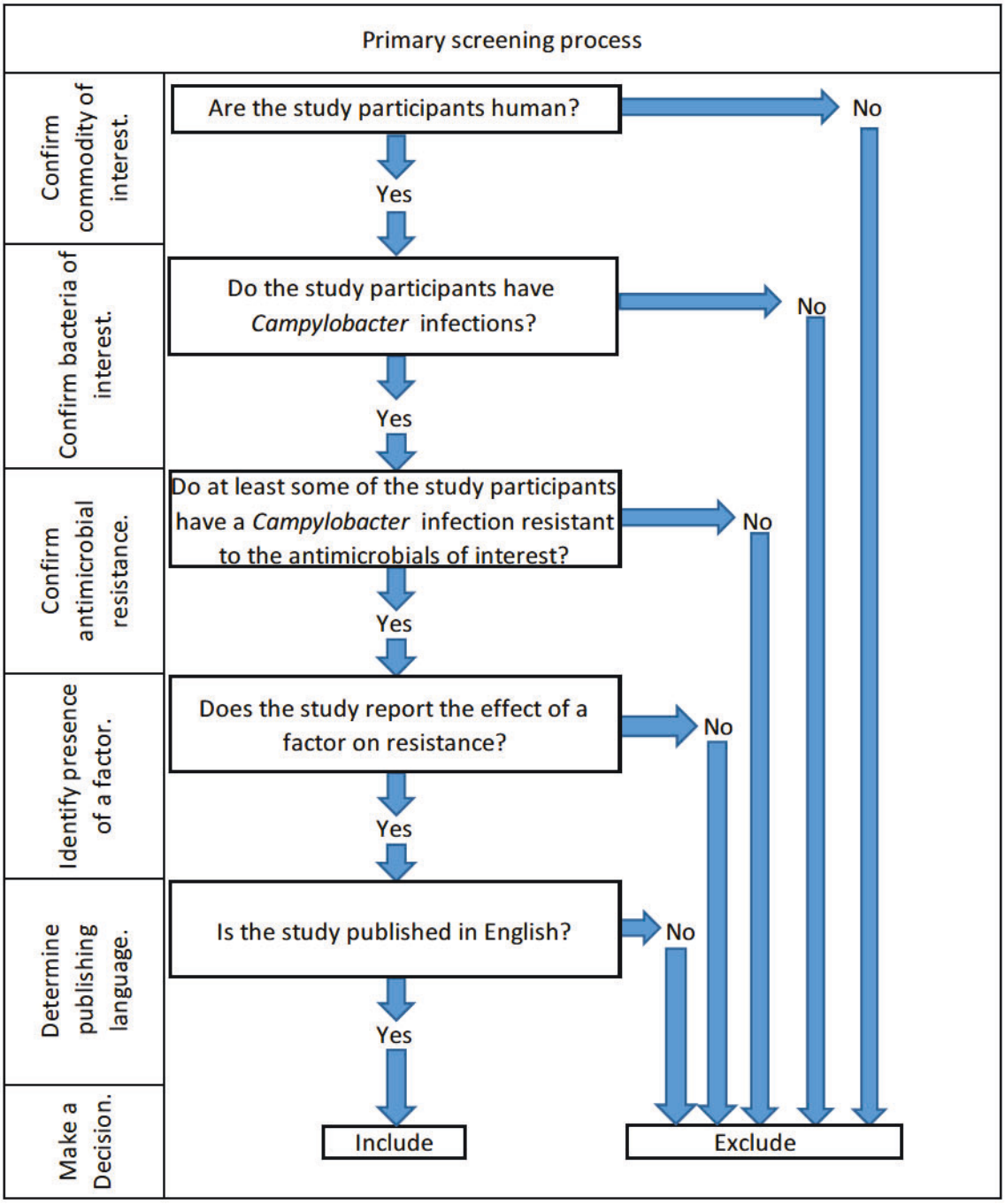
Search Strategy

An initial limited search was completed in MEDLINE® in Ovid using a preliminary search string (13-15). An informal analysis of terms used in the title, abstract and index was conducted and relevant terms were included in the search string. The final search string, see appendix, will be adapted and applied across all of the following databases: AGRICOLA™ in ProQuest®, Centre for Agriculture and Bioscience abstracts in Web of Science, EMBASE® in Ovid, Scopus®, and MEDLINE® in Ovid. Grey literature sources to be searched will be the World Health Organization's Global Index Medicus, and the Bielefield Academic Search Engine. Additionally, the first 250 results, sorted based on relevance, from Google Scholar will also be screened for eligibility. Lastly, the lists of references from the included studies will be reviewed to identify any additional relevant articles.

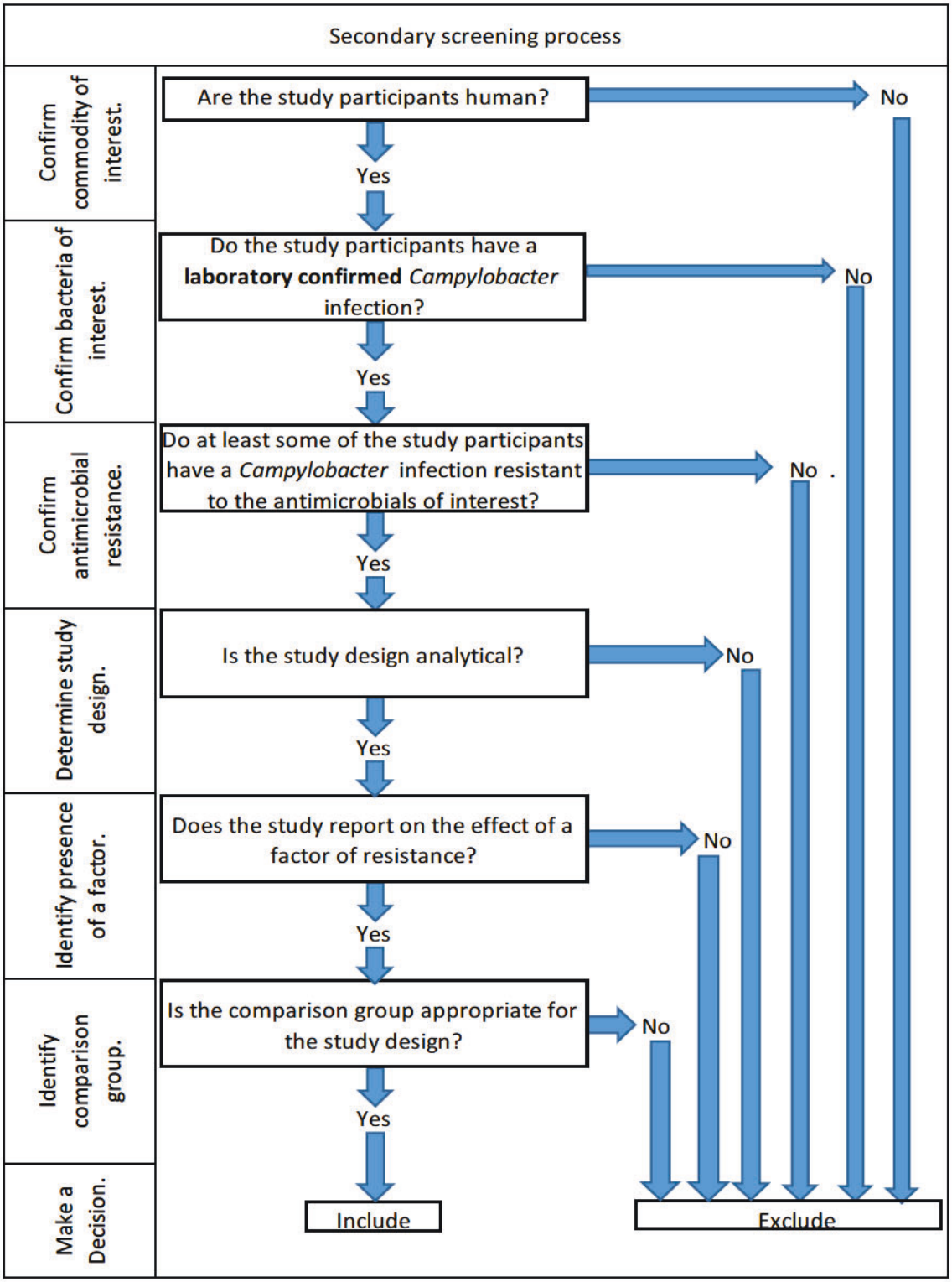
Study Selection

The primary screening will be conducted on the title and abstract of each article. The following questions will be used in the primary screening process:

1. Does the title and/or abstract indicate the study subjects are human?
2. Does the title and/or abstract indicate the study participants have *Campylobacter* infections?
3. Does the title and/or abstract indicate at least some of the study participants have a *Campylobacter* infection that is resistant to the antimicrobials of interest?
4. Does the title and/or abstract indicate that the study reports on the effect of a factor on resistance?
5. Is the study published in English?



The primary screening will be performed by two researchers. The possible answers are yes, no, an unclear. If the article fully or partially meets the inclusion criteria (i.e. all screening questions are answered either 'yes' or 'unclear'), the article will proceed to secondary screening. Reasons for exclusion will be indicated. For both primary and secondary screening, the answers will be compared and any disagreements will be discussed until consensus is achieved. If consensus cannot be reached, then a third researcher will be used to arbitrate.



The secondary screening will be performed on the full text articles. The following questions will be used for the secondary screening:

1. Are study subjects are human?
2. Do the study participants have a laboratory confirmed *Campylobacter* infection?

3. Do at least some of the study participants have a *Campylobacter* infection that is resistant to the antimicrobials of interest?
4. Is the study design analytical?
5. Does the study report on the effect of a factor on resistance?
6. Is the comparison group appropriate for the study design?

The secondary screening will be performed independently by two researchers. The possible answers are 'yes' or 'no'. For an article to be included, all of the above questions must be answered with a 'yes'. One or more answers of 'no' to the questions above leads to exclusion of the article and information regarding the reason for exclusion will be recorded.

Data Extraction

EndNote X9™ will be used for managing citations. All eligible articles will be uploaded onto EndNote X9™ and any duplicates will be removed. The remaining articles will then be uploaded onto DistillerSR® and checked again for duplicates. Screening forms will be created using the software and will be used to determine eligibility.

A data extraction form will be created in DistillerSR®. Data extracted will include:

- Characteristics of the study, including:
  - Year of publication
  - Type of document
  - Author report study design
  - Year(s) data were collected
  - Country or countries study was performed in
  - Methods used
- Characteristics of the study participants, including:
  - Population
  - Sample size
- Description of and results for factor(s) investigated, including:
  - Count and rate data
  - Measures of association and variation
  - Definition of factor(s) investigated
  - Associated results and key findings

Presentation of Results

Results will be presented using a narrative summary with the inclusion of tables and summaries of results as is warranted. Narrative summaries will be completed for each type of resistance of interest. Tables will include characteristics of the studies, characteristics of the participants, and the factors investigated.

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APPROVED

By Christine Neustaedter at 5:56 pm, Feb 04, 2020

Appendix

Ovid MEDLINE®	
#	Searches
1	Campylobacter$.ab,kf,ti. or exp Campylobacter/
2	exp Drug Resistance, Microbial/ or resistan$.ab,kf,ti.
3	(Chlortetracycline$ or clomocycline$ or demeclocycline$ or doxycycline$ or eravacycline$ or lymecycline$ or metacycline$ or minocycline$ or omadacycline$ or oxytetracycline$ or penimepicycline$ or rolitetracycline$ or tetracycline$).ab,kf,ti.
4	(azithromycin$ or cethromycin$ or clarithromycin$ or dirithromycin$ or erythromycin$ or fidaxomicin$ or flurithromycin$ or gamithromycin$ or josamycin$ or kitasamycin$ or midecamycin$ or miocamycin$ or oleandomycin$ or rokitamycin$ or roxithromycin$ or spiramycin$ or telithromycin$ or tildipirosin$ or tilmicosin$ or troleandomycin$ or solithromycin$ or tulathromycin$ or tylosin$ or tylvalosin$ or macrolide$).ab,kf,ti.
5	(besifloxacin$ or cinoxacin$ or ciprofloxacin$ or danofloxacin$ or delafloxacin$ or difloxacin$ or enoxacin$ or enrofloxacin$ or fleroxacin$ or flumequine$ or garenoxacin$ or gatifloxacin$ or gemifloxacin$ or grepafloxacin$ or ibafloxacin$ or levofloxacin$ or lomefloxacin$ or marbofloxacin$ or moxifloxacin$ or nadifloxacin$ or nalidixic acid or norfloxacin$ or ofloxacin$ or orbifloxacin$ or ozenoxacin$ or oxolinic acid or pazufloxacin$ or pefloxacin$ or pipemidic acid or piromidic acid or pradofloxacin$ or prulifloxacin$ or rosoxacin$ or rufloxacin$ or sitafloxacin$ or sparfloxacin$ or temafloxacin$ or quinolone$ or fluoroquinolone$).ab,kf,ti.
6	Drug Resistance, Multiple, Bacterial/ or (MDR or XDR or PDR or important antimicrobial$ or important antibiotic$).ab,kf,ti.
7	2 or 3 or 4 or 5 or 6
8	1 and 7
9	8 not (Animal/ not (Animal/ and Human/))

Note: Search string development used references 13-15

ProQuest ® AGRICOLA™	
#	Searches
1	noft(Campylobacter*)
2	noft("Drug Resistance" or resistan*)
3	noft(Chlortetracycline* or clomocycline* or demeclocycline* or doxycycline* or eravacycline* or lymecycline* or metacycline* or minocycline* or omadacycline* or oxytetracycline* or penimepicycline* or rolitetracycline* or tetracycline*)
4	noft(azithromycin* or cethromycin* or clarithromycin* or dirithromycin* or erythromycin* or fidaxomicin* or flurithromycin* or gamithromycin* or josamycin* or kitasamycin* or midecamycin* or miocamycin* or oleandomycin* or rokitamycin* or roxithromycin* or spiramycin* or telithromycin* or tildipirosin* or tilmicosin* or troleandomycin* or solithromycin* or tulathromycin* or tylosin* or tylvalosin* or macrolide*)
5	noft(besifloxacin* or cinoxacin* or ciprofloxacin* or danofloxacin* or delafloxacin* or difloxacin* or enoxacin* or enrofloxacin* or fleroxacin* or

	flumequine* or garenoxacin* or gatifloxacin* or gemifloxacin* or grepafloxacin* or ibafloxacin* or levofloxacin* or lomefloxacin* or marbofloxacin* or moxifloxacin* or nadifloxacin* or nalidixic acid or norfloxacin* or ofloxacin* or orbifloxacin* or ozenoxacin* or oxolinic acid or pazufloxacin* or pefloxacin* or pipemidic acid or piromidic acid or pradofloxacin* or prulifloxacin* or rosoxacin* or rufloxacin* or sitafloxacin* or sparfloxacin* or temafloxacin* or quinolone* or fluoroquinolone*)
6	noft(MDR or XDR or PDR or "important antimicrobial*" or "important antibiotic*")
7	S2 or S3 or S4 or S5 or S6
8	S1 and S7
9	S8 NOT (noft(nonhuman* or animal*) NOT noft(((human*) AND ((nonhuman*) OR ("animal*")))))

Web of Science: CABI: CAB Abstracts® and Global Health®	
#	Searches
1	TS=(Campylobacter*) or DE=(Campylobacter*)
2	TS=("Drug Resistance" or resistan*) or DE=("drug resistance")
3	TS=(Chlortetracycline* or clomocycline* or demeclocycline* or doxycycline* or eravacycline* or lymecycline* or metacycline* or minocycline* or omadacycline* or oxytetracycline* or penimepicycline* or rolitetracycline* or tetracycline*)
4	TS=(azithromycin* or cethromycin* or clarithromycin* or dirithromycin* or erythromycin* or fidaxomicin* or flurithromycin* or gamithromycin* or josamycin* or kitasamycin* or midecamycin* or miocamycin* or oleandomycin* or rokitamycin* or roxithromycin* or spiramycin* or telithromycin* or tildipirosin* or tilmicosin* or troleandomycin* or solithromycin* or tulathromycin* or tylosin* or tylvalosin* or macrolide*)
5	TS=(besifloxacin* or cinoxacin* or ciprofloxacin* or danofloxacin* or delafloxacin* or difloxacin* or enoxacin* or enrofloxacin* or fleroxacin* or flumequine* or garenoxacin* or gatifloxacin* or gemifloxacin* or grepafloxacin* or ibafloxacin* or levofloxacin* or lomefloxacin* or marbofloxacin* or moxifloxacin* or nadifloxacin* or nalidixic acid or norfloxacin* or ofloxacin* or orbifloxacin* or ozenoxacin* or oxolinic acid or pazufloxacin* or pefloxacin* or pipemidic acid or piromidic acid or pradofloxacin* or prulifloxacin* or rosoxacin* or rufloxacin* or sitafloxacin* or sparfloxacin* or temafloxacin* or quinolone* or fluoroquinolone*)
6	TS=(MDR or XDR or PDR or "important antimicrobial*" or "important antibiotic*") or DE=("multiple drug resistance")
7	#2 or #3 or #4 or #5 or #6
8	#1 and #7
9	((TS=animal* NOT (TS=(animal* AND human*))))
10	#8 NOT #9

Ovid EMBASE®	
#	Searches
1	campylobacter$.ab,kw,ti. or exp campylobacter/
2	exp antibiotic resistance/ or resistan$.ab,kw,ti.
3	(chlortetracycline$ or clomocycline$ or demeclocycline$ or doxycycline$ or eravacycline$ or lymecycline$ or metacycline$ or minocycline$ or

	omadacycline$ or oxytetracycline$ or penimepicycline$ or rolitetracycline$ or tetracycline$).ab,kw,ti.
4	(azithromycin$ or cethromycin$ or clarithromycin$ or dirithromycin$ or erythromycin$ or fidaxomicin$ or flurithromycin$ or gamithromycin$ or josamycin$ or kitasamycin$ or midecamycin$ or miocamycin$ or oleandomycin$ or rokitamycin$ or roxithromycin$ or spiramycin$ or telithromycin$ or tildipirosin$ or tilmicosin$ or troleandomycin$ or solithromycin$ or tulathromycin$ or tylosin$ or tylvalosin$ or macrolide$).ab,kw,ti.
5	(besifloxacin$ or cinoxacin$ or ciprofloxacin$ or danofloxacin$ or delafloxacin$ or difloxacin$ or enoxacin$ or enrofloxacin$ or fleroxacin$ or flumequine$ or garenoxacin$ or gatifloxacin$ or gemifloxacin$ or grepafloxacin$ or ibafloxacin$ or levofloxacin$ or lomefloxacin$ or marbofloxacin$ or moxifloxacin$ or nadifloxacin$ or nalidixic acid or norfloxacin$ or ofloxacin$ or orbifloxacin$ or ozenoxacin$ or oxolinic acid or pazufloxacin$ or pefloxacin$ or pipemidic acid or piromidic acid or pradofloxacin$ or prulifloxacin$ or rosoxacin$ or rufloxacin$ or sitafloxacin$ or sparfloxacin$ or temafloxacin$ or quinolone$ or fluoroquinolone$).ab,kw,ti.
6	exp multidrug resistance/ or (MDR or XDR or PDR or important antimicrobial$ or important antibiotic$).ab,kw,ti.
7	2 or 3 or 4 or 5 or 6
8	1 and 7
9	8 NOT ((exp animal/ or nonhuman/) not exp human/)

Scopus®	
#	Searches
1	TITLE-ABS-KEY(Campylobacter*)
2	TITLE-ABS-KEY("Drug Resistance" or resistan*)
3	TITLE-ABS-KEY(Chlortetracycline* or clomocycline* or demeclocycline* or doxycycline* or eravacycline* or lymecycline* or metacycline* or minocycline* or omadacycline* or oxytetracycline* or penimepicycline* or rolitetracycline* or tetracycline*)
4	TITLE-ABS-KEY(azithromycin* or cethromycin* or clarithromycin* or dirithromycin* or erythromycin* or fidaxomicin* or flurithromycin* or gamithromycin* or josamycin* or kitasamycin* or midecamycin* or miocamycin* or oleandomycin* or rokitamycin* or roxithromycin* or spiramycin* or telithromycin* or tildipirosin* or tilmicosin* or troleandomycin* or solithromycin* or tulathromycin* or tylosin* or tylvalosin* or macrolide*)
5	TITLE-ABS-KEY(besifloxacin* or cinoxacin* or ciprofloxacin* or danofloxacin* or delafloxacin* or difloxacin* or enoxacin* or enrofloxacin* or fleroxacin* or flumequine* or garenoxacin* or gatifloxacin* or gemifloxacin* or grepafloxacin* or ibafloxacin* or levofloxacin* or lomefloxacin* or marbofloxacin* or moxifloxacin* or nadifloxacin* or "nalidixic acid" or norfloxacin* or ofloxacin* or orbifloxacin* or ozenoxacin* or "oxolinic acid" or pazufloxacin* or pefloxacin* or "pipemidic acid" or "piromidic acid" or pradofloxacin* or prulifloxacin* or rosoxacin* or rufloxacin* or sitafloxacin* or sparfloxacin* or temafloxacin* or quinolone* or fluoroquinolone*)
6	TITLE-ABS-KEY(MDR or XDR or PDR or "important antimicrobial*" or "important antibiotic*")
7	#2 or #3 or #4 or #5 or #6

8	#1 and #7
9	TITLE-ABS-KEY(animal*) AND NOT (TITLE-ABS-KEY(animal* AND human*))
10	#8 AND NOT #9

Grey Literature	
Search Engine	Search String
Google Scholar	campylobacter* AND (resistance or fluoroquinolone or macrolide or tetracycline)
Global Index Medicus (WHO)	campylobacter* AND (resistance or fluoroquinolone or tetracycline or macrolide)
Bielefield Academic Search Engine	((campylobacter*) AND (resistance fluoroquinolone macrolide tetracycline)) NOT (animal* NOT (human* AND animal*))

APPENDIX 2.2

All Extracted Data from Scoping Review

[In the following pages]

Factor ID	Paper REF	Year	What year(s) were the data collected? (format: mm/dd/yy-mm/dd/yy)	What is the study design?	How was participant information collected?	What is/are the study objectives?	What is the method used for antimicrobial susceptibility testing-Combined	What MIC interpretive criteria was used?	What country was the study population included from?	What was the population(s) sampled?	What was the total sample size?
1	Bottieau, 2011	2011	04/--/00-09/--/06	Prospective cohort	Observation	To review the epidemiology, clinical presentation, resistance pattern and outcome of invasive bacterial enteritis in the subset of patients diagnosed with febrile traveller's diarrhoea.	Disk Diffusion	"defined according to international recommendations"	Belgium	Travellers in Belgium between April 2000 and September 2006 presenting with fever after a stay in the tropics or subtropics (defined as any non-industrialized country at least partly situated between the 35 degree northern and 35 degree southern latitude)	1730
2	Engberg, 2004	2004	12/01/01-06/10/02	Case-control	Observation	To identify risk factors associated with acquiring quinolone-resistant C. jejuni infections	Disk Diffusion	nalidixic acid MIC>64 mg/L and a zone size of less than or equal 27 mm for the tablet method	Denmark	Sampled from a larger prospective cohort that involved all culture-positive campylobacter infections from May 1, 2001 to June 10, 2002 from the counties of Copenhagen and Funen.	126
3	Engberg, 2004	2004	12/01/01-06/10/02	Case-control	Observation	To identify risk factors associated with acquiring quinolone-resistant C. jejuni infections	Disk Diffusion	nalidixic acid MIC>64 mg/L and a zone size of less than or equal 27 mm for the tablet method	Denmark	Sampled from a larger prospective cohort that involved all culture-positive campylobacter infections from May 1, 2001 to June 10, 2002 from the counties of Copenhagen and Funen.	126
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12	Evans, 2009	2009	04/--/03-09/--/04	Case-control	Survey/Questionnaire	To identify risk factors for ciprofloxacin-resistant Campylobacter infection. Null hypothesis that there was no difference between case and comparison patients in exposure to several variables. The study aimed to achieve a 90% power to detect an odds ratio of 2.5 assuming a 10% exposure frequency and 0.05 significance level	Disk Diffusion	BSAC [resistant zone less than or equal to 17mm, MIC= greater than or equal to 4 milligrams/L)	United Kingdom	Patients between April 2003 and September 2004 recruited through the Welsh laboratory surveillance scheme only form laboratories that routinely tested all Campylobacter species for ciprofloxacin resistance.	556
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47	Feodoroff, 2010	2010	07/01/06-12/31/06	Cross-sectional	Survey/Questionnaire	To reveal other bacterial factors that may affect the outcome material including both infections acquired abroad or in Finland	Not Specified	CLSI clinical breakpoints	Finland	People in Finland with confirmed Campylobacter during the specified time period	166
48	Gallay, 2008	2007	09/15/02-06/30/04	Case-Case-Control	Survey/Questionnaire	To better document the risk factors for sporadic Campylobacter infection in France	Agar Diffusion	Antibiogram Committee of the French Society for Microbiology	France	French people from 2002-2004	570
49	Gallay, 2008	2007	09/15/02-06/30/04	Case-Case-Control	Survey/Questionnaire	To better document the risk factors for sporadic Campylobacter infection in France	Agar Diffusion	Antibiogram Committee of the French Society for Microbiology	France	French people from 2002-2004	570

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50	Gaudreau, 2003	2003	12/--/99-11/--/01	retrospective cohort	Patient file review	Our study aimed to confirm the presence of such an outbreak of antibiotic resistant C. jejuni enterocolitis in the male population of Montreal and to determine the susceptibility of these isolates to 6 other antimicrobial agents.	Disk Diffusion, Agar Dilution, and E-test	Erythro (>126 micrograms/mL), Azithro(Resistant), Cipr(4 micrograms/mL), Nalidixic acid (Resistant), Amoxicillin-Calvulanic acid, Imipenem, and meropenem (<=0.06 micrograms/mL), gentamicin (0.5 micrograms/mL), Tetracycline (0.25micrograms/mL)	Canada	Men in Montreal between the dates listed	14
51	Gaudreau, 2003	2003	12/--/99-11/--/01	retrospective cohort	Patient file review	Our study aimed to confirm the presence of such an outbreak of antibiotic resistant C. jejuni enterocolitis in the male population of Montreal and to determine the susceptibility of these isolates to 6 other antimicrobial agents.	Disk Diffusion, Agar Dilution, and E-test	Erythro (>126 micrograms/mL), Azithro(Resistant), Cipr(4 micrograms/mL), Nalidixic acid (Resistant), Amoxicillin-Calvulanic acid, Imipenem, and meropenem (<=0.06 micrograms/mL), gentamicin (0.5 micrograms/mL), Tetracycline (0.25micrograms/mL)	Canada	Men in Montreal between the dates listed	14
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52	Gaudreau, 2003	2003	12/--/99-11/--/01	retrospective cohort	Patient file review	Our study aimed to confirm the presence of such an outbreak of antibiotic resistant C. jejuni enterocolitis in the male population of Montreal and to determine the susceptibility of these isolates to 6 other antimicrobial agents.	Disk Diffusion, Agar Dilution, and E-test	Erythro (>126 micrograms/mL), Azithro(Resistant), Cipr(4 micrograms/mL), Nalidixic acid (Resistant), Amoxicillin-Calvulanic acid, Imipenem, and meropenem (<=0.06 micrograms/mL), gentamicin (0.5 micrograms/mL), Tetracycline (0.25micrograms/mL)	Canada	Men in Montreal between the dates listed	14
53	Gaudreau, 2015	2015	01/01/03-12/31/13	retrospective cohort	Patient file review	To investigate an outbreak of sexual transmission of 2 clades of AMR C. jejuni in men who have sex with men in Quebec, Canada	Disk Diffusion, Agar Dilution, and E-test	Not Reported	Canada	Men in Quebec, Canada	31
54	Gaudreau, 2015	2015	01/01/03-12/31/13	retrospective cohort	Patient file review	To investigate an outbreak of sexual transmission of 2 clades of AMR C. jejuni in men who have sex with men in Quebec, Canada	Disk Diffusion, Agar Dilution, and E-test	Not Reported	Canada	Men in Quebec, Canada	31
55	Gaudreau, 2015	2015	01/01/03-12/31/13	retrospective cohort	Patient file review	To investigate an outbreak of sexual transmission of 2 clades of AMR C. jejuni in men who have sex with men in Quebec, Canada	Disk Diffusion, Agar Dilution, and E-test	Not Reported	Canada	Men in Quebec, Canada	31
56	Gaudreau, 2015	2015	01/01/03-12/31/13	retrospective cohort	Patient file review	To investigate an outbreak of sexual transmission of 2 clades of AMR C. jejuni in men who have sex with men in Quebec, Canada	Disk Diffusion, Agar Dilution, and E-test	Not Reported	Canada	Men in Quebec, Canada	31
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57	Ghunaim, 2015	2015	2005-2013	Cross-sectional	Patient file review	To investigate the prevalence and association of antimicrobial resistance and virulence factors among C. jejuni isolates from symptomatic patients presenting as out-patients at the HMC hospital in order to enable knowledge based informed decisions relevant to the continuously changing dynamics of this society to be made by local health professionals and policy makers.	E-test	CLSI clinical breakpoints	United Kingdom	People of the United Kingdom during the specified years with severe and bloody diarrhea	174
58	Ghunaim, 2015	2015	2005-2013	Cross-sectional	Patient file review	To investigate the prevalence and association of antimicrobial resistance and virulence factors among C. jejuni isolates from symptomatic patients presenting as out-patients at the HMC hospital in order to enable knowledge based informed decisions relevant to the continuously changing dynamics of this society to be made by local health professionals and policy makers.	E-test	CLSI clinical breakpoints	United Kingdom	People of the United Kingdom during the specified years with severe and bloody diarrhea	174
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62	Ghunaim, 2015	2015	2005-2013	Cross-sectional	Patient file review	To investigate the prevalence and association of antimicrobial resistance and virulence factors among C. jejuni isolates from symptomatic patients presenting as out-patients at the HMC hospital in order to enable knowledge based informed decisions relevant to the continuously changing dynamics of this society to be made by local health professionals and policy makers.	E-test	CLSI clinical breakpoints	United Kingdom	People of the United Kingdom during the specified years with severe and bloody diarrhea	174
63	Hakanen, 2003	2003	01/--/95-11/--/97 and 10/--/98-01/--/00	Cross-sectional	Observation	To evaluate the level of fluoroquinolone resistance in C. jejuni isolates from travelers returning to Finland and to specify the countries were resistant isolates are acquire	Agar Dilution	NCCLS	Finland	Travelers returning to Finland from 1995 to 2000	354
64	Hakanen, 2003	2003	01/--/95-11/--/97 and 10/--/98-01/--/00	Cross-sectional	Observation	To evaluate the level of fluoroquinolone resistance in C. jejuni isolates from travelers returning to Finland and to specify the countries were resistant isolates are acquire	Agar Dilution	NCCLS	Finland	Travelers returning to Finland from 1995 to 2000	354
65	Hakanen, 2003	2003	01/--/95-11/--/97 and 10/--/98-01/--/00	Cross-sectional	Observation	To evaluate the level of fluoroquinolone resistance in C. jejuni isolates from travelers returning to Finland and to specify the countries were resistant isolates are acquire	Agar Dilution	NCCLS	Finland	Travelers returning to Finland from 1995 to 2000	354
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68	Hakanen, 2003	2003	01/--/95-11/--/97 and 10/--/98-01/--/00	Cross-sectional	Observation	To evaluate the level of fluoroquinolone resistance in C. jejuni isolates from travelers returning to Finland and to specify the countries were resistant isolates are acquire	Agar Dilution	NCCLS	Finland	Travelers returning to Finland from 1995 to 2000	354
69	Helms, 2005	2005	01/01/96-12/01/00	Cohort	Patient file review	To determine the risk of invasive illness or death associated with quinolone or erythromycin resistance in campylobacter strains	Disk Diffusion	<27mm for nalidixic acid or erythromycin	Denmark	All citizens of Denmark between the specified dates	3541
70	Helms, 2005	2005	01/01/96-12/01/00	Cohort	Patient file review	To determine the risk of invasive illness or death associated with quinolone or erythromycin resistance in campylobacter strains	Disk Diffusion	<27mm for nalidixic acid or erythromycin	Denmark	All citizens of Denmark between the specified dates	3541
71	Jenkin, 1998	1998	10/--/88-04/--/96	Cross-sectional	Patient file review	To describe 19 HIV-infected patients who were culture-positive for C. upsaliensis and review the clinical and bacteriologic features and outcomes of these cases.	Disk Diffusion	Not Reported	Australia	Adult HIV-infected patients at Fairfield hospital with stool specimens before it's closure in May 1996	20
72	Johnson, 2008	2007	02/01/04-07/29/05	Case-control	Survey/Questionnaire	To investigate the relative importance of a number of risk factors for ciprofloxacin resistance in Campylobacter infections	Disk Diffusion	5 micrograms of ciprofloxacin inhibition zone: <= 15 mm resistant; 16-20 mm intermediate; >= 21 mm susceptible. Nalidixic acid zone diamter >= 20 mm	Canada	Residents of the Chinook Health Region and Calgary Health Region, Alberta, Canada, greater than 16 years old,	210
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74	Johnson, 2008	2007	02/01/04-07/29/05	Case-control	Survey/Questionnaire	To investigate the relative importance of a number of risk factors for ciprofloxacin resistance in Campylobacter infections	Disk Diffusion	5 micrograms of ciprofloxacin inhibition zone: <= 15 mm resistant; 16-20 mm intermediate; >= 21 mm susceptible. Nalidixic acid zone diamter >= 20 mm	Canada	Residents of the Chinook Health Region and Calgary Health Region, Alberta, Canada, greater than 16 years old,	210
75	Johnson, 2008	2007	02/01/04-07/29/05	Case-control	Survey/Questionnaire	To investigate the relative importance of a number of risk factors for ciprofloxacin resistance in Campylobacter infections	Disk Diffusion	5 micrograms of ciprofloxacin inhibition zone: <= 15 mm resistant; 16-20 mm intermediate; >= 21 mm susceptible. Nalidixic acid zone diamter >= 20 mm	Canada	Residents of the Chinook Health Region and Calgary Health Region, Alberta, Canada, greater than 16 years old,	210
76	Johnson, 2008	2007	02/01/04-07/29/05	Case-control	Survey/Questionnaire	To investigate the relative importance of a number of risk factors for ciprofloxacin resistance in Campylobacter infections	Disk Diffusion	5 micrograms of ciprofloxacin inhibition zone: <= 15 mm resistant; 16-20 mm intermediate; >= 21 mm susceptible. Nalidixic acid zone diamter >= 20 mm	Canada	Residents of the Chinook Health Region and Calgary Health Region, Alberta, Canada, greater than 16 years old,	210
77	Johnson, 2008	2007	02/01/04-07/29/05	Case-control	Survey/Questionnaire	To investigate the relative importance of a number of risk factors for ciprofloxacin resistance in Campylobacter infections	Disk Diffusion	5 micrograms of ciprofloxacin inhibition zone: <= 15 mm resistant; 16-20 mm intermediate; >= 21 mm susceptible. Nalidixic acid zone diamter >= 20 mm	Canada	Residents of the Chinook Health Region and Calgary Health Region, Alberta, Canada, greater than 16 years old,	210
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79	Johnson, 2008	2007	02/01/04-07/29/05	Case-control	Survey/Questionnaire	To investigate the relative importance of a number of risk factors for ciprofloxacin resistance in Campylobacter infections	Disk Diffusion	5 micrograms of ciprofloxacin inhibition zone: <= 15 mm resistant; 16-20 mm intermediate; >= 21 mm susceptible. Nalidixic acid zone diamter >= 20 mm	Canada	Residents of the Chinook Health Region and Calgary Health Region, Alberta, Canada, greater than 16 years old,	210
80	Johnson, 2008	2007	02/01/04-07/29/05	Case-control	Survey/Questionnaire	To investigate the relative importance of a number of risk factors for ciprofloxacin resistance in Campylobacter infections	Disk Diffusion	5 micrograms of ciprofloxacin inhibition zone: <= 15 mm resistant; 16-20 mm intermediate; >= 21 mm susceptible. Nalidixic acid zone diamter >= 20 mm	Canada	Residents of the Chinook Health Region and Calgary Health Region, Alberta, Canada, greater than 16 years old,	210
81	Koningstein, 2011	2011	1999-2005	Cross-sectional	Patient file review	To evaluate the association between fluoroquinolones and macrolides prescribed in general practice on the occurrence of subsequent infection as well as to estimate the odds of diagnosis with a resistant strain after exposure to a course of antimicrobials	Not Specified	CLSI clinical breakpoints	Denmark	The population of Denmark between the specified years	10475
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83	Kownhar, 2007	2007	04/--/01-03/--/04	Case-Control	Observation	To compare the prevalence of C.jejuni among HIV-infected and non-HIV infected patients	Disk Diffusion	NCCLS	India	People with diarrhea in Chennai, India between the study dates, >=18 years of age, male or female	400
84	Kownhar, 2007	2007	04/--/01-03/--/04	Case-Control	Observation	To compare the prevalence of C.jejuni among HIV-infected and non-HIV infected patients	Disk Diffusion	NCCLS	India	People with diarrhea in Chennai, India between the study dates, >=18 years of age, male or female	400
85	Kownhar, 2007	2007	04/--/01-03/--/04	Case-Control	Observation	To compare the prevalence of C.jejuni among HIV-infected and non-HIV infected patients	Disk Diffusion	NCCLS	India	People with diarrhea in Chennai, India between the study dates, >=18 years of age, male or female	400
86	Kownhar, 2007	2007	04/--/01-03/--/04	Case-Control	Observation	To compare the prevalence of C.jejuni among HIV-infected and non-HIV infected patients	Disk Diffusion	NCCLS	India	People with diarrhea in Chennai, India between the study dates, >=18 years of age, male or female	400
87	Kownhar, 2007	2007	04/--/01-03/--/04	Case-Control	Observation	To compare the prevalence of C.jejuni among HIV-infected and non-HIV infected patients	Disk Diffusion	NCCLS	India	People with diarrhea in Chennai, India between the study dates, >=18 years of age, male or female	400
88	Lu, 2000	2000	01/--/91-03/--/99	retrospective cohort	Patient file review	To determine the clinical characteristics of patients with Campylobacter infection in a university hospital in Taiwan and the antimicrobial susceptibility patterns of the Campylobacter isolates	E-test	NCCLS	Taiwan	Patients with Campylobacter bacteremia in the National Taiwan University Hospital during the dates specified above	21
89	Nelson, 2004	2004	02/--/98-01/--/99	Case-control	Survey/Questionnaire	To determine whether persons with ciprofloxacin-resistant campylobacter infection have a more sever or porlonged illness than do persons with ciprofloxacin-susceptible campylobacter infection	E-test	>=4 micrograms/mL	United States	People in the United States with campylobacter	740
Factor ID	Paper REF	Year	What year(s) were the data collected? (format: mm/dd/yy-mm/dd/yy)	What is the study design?	How was participant information collected?	What is/are the study objectives?	What is the method used for antimicrobial susceptibility testing-Combined	What MIC interpretive criteria was used?	What country was the study population included from?	What was the population(s) sampled?	What was the total sample size?

90	Nelson, 2004	2004	02/--/98-01/--/99	Case-control	Survey/Questionnaire	To determine whether persons with ciprofloxacin-resistant campylobacter infection have a more sever or porlonged illness than do persons with ciprofloxacin-susceptible campylobacter infection	E-test	>=4 micrograms/mL	United States	People in the United States with campylobacter	740
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96	Patrick, 2018	2018	2010-2015	Cross-sectional	Patient file review	To provide a comprehensive description of campylobacter cases at the species level in the USA	Not Specified	NARMS	United States	United States Citizens during the study years	16549
97	Patrick, 2018	2018	2010-2015	Cross-sectional	Patient file review	To provide a comprehensive description of campylobacter cases at the species level in the USA	Not Specified	NARMS	United States	United States Citizens during the study years	16549
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100	Patrick, 2018	2018	2010-2015	Cross-sectional	Patient file review	To provide a comprehensive description of campylobacter cases at the species level in the USA	Not Specified	NARMS	United States	United States Citizens during the study years	16549
101	Patrick, 2018	2018	2010-2015	Cross-sectional	Patient file review	To provide a comprehensive description of campylobacter cases at the species level in the USA	Not Specified	NARMS	United States	United States Citizens during the study years	16549
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103	Perlman, 1988	1988	--/--/85---/--/86	Cohort	Patient file review	To describe four HIV-infected patients with C. jejuni infections	Agar Dilution	Not Reported	United States	Patients with HIV	4
104	Ricotta, 2014	2014	2005-2011	Cross-sectional	Patient file review	To determine the role international travel plays in US Campylobacter epidemiologically and antimicrobial resistance.	Not Specified	NARMS	United States	United states population with campylobacter	24 433
105	Ricotta, 2014	2014	2005-2011	Cross-sectional	Patient file review	To determine the role international travel plays in US Campylobacter epidemiologically and antimicrobial resistance.	Not Specified	NARMS	United States	United states population with campylobacter	24 433
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107	Ricotta, 2014	2014	2005-2011	Cross-sectional	Patient file review	To determine the role international travel plays in US Campylobacter epidemiologically and antimicrobial resistance.	Not Specified	NARMS	United States	United states population with campylobacter	24 433
108	Sharma, 2003	2003	01/--/99-07/--/01	Case-control	Survey/Questionnaire	To describe antibiotic resistance profiles of human campylobacter isolates and evaluate multiple typing methods for their usefulness to examine specific risk factors for campylobacter infection	Agar Dilution	NCCLS	Australia	Population of the Hunter region of New South Wales during the specified dates	155
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111	Sharma, 2003	2003	01/--/99-07/--/01	Case-control	Survey/Questionnaire	To describe antibiotic resistance profiles of human campylobacter isolates and evaluate multiple typing methods for their usefulness to examine specific risk factors for campylobacter infection	Agar Dilution	NCCLS	Australia	Population of the Hunter region of New South Wales during the specified dates	155
112	Skjot-Rasmussen, 2009	2009	1997-2007	Cross-sectional	Survey/Questionnaire	To look at trends in occurrence of resistance among C. jejuni isolated from broiler chickens, broiler chicken meat, and human domestically acquired cases and travel associated cases in Denmark from 1997 to 2007.	Disk Diffusion, Agar Dilution	Ciprofloxacin <27 mm, erythromycin <27 mm, nalidixic acid <27 mm, and tetracycline <32 mm.	Denmark	Danish domestically acquired human cases of campylobacter and travel associated human cases	1023
113	Skjot-Rasmussen, 2009	2009	1997-2007	Cross-sectional	Survey/Questionnaire	To look at trends in occurrence of resistance among C. jejuni isolated from broiler chickens, broiler chicken meat, and human domestically acquired cases and travel associated cases in Denmark from 1997 to 2007.	Disk Diffusion, Agar Dilution	Ciprofloxacin <27 mm, erythromycin <27 mm, nalidixic acid <27 mm, and tetracycline <32 mm.	Denmark	Danish domestically acquired human cases of campylobacter and travel associated human cases	1023
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115	Smith, 1999	1999	1992-1997	Case-control	Survey/Questionnaire	To analyze recent trends in quinolone-resistant campylobacter infections, risk factors for infection with resistant organisms, and poultry as a potential source of resistant organisms.	Disk Diffusion, E-test	NCCLS	United States	People in Minnesota during the specified years	390
116	Smith, 1999	1999	1992-1997	Case-control	Survey/Questionnaire	To analyze recent trends in quinolone-resistant campylobacter infections, risk factors for infection with resistant organisms, and poultry as a potential source of resistant organisms.	Disk Diffusion, E-test	NCCLS	United States	People in Minnesota during the specified years	390
117	Smith, 1999	1999	1992-1997	Case-control	Survey/Questionnaire	To analyze recent trends in quinolone-resistant campylobacter infections, risk factors for infection with resistant organisms, and poultry as a potential source of resistant organisms.	Disk Diffusion, E-test	NCCLS	United States	People in Minnesota during the specified years	390
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125	Moore, 2002	2002	Not Specified	Cross-sectional	Patient file review	To compare antibiotic resistant strains, particularly fluoroquinolone-resistant organisms, from human clinical sources and chickens originating in Northern Ireland over a similar time period	Disk Diffusion, E-test	Not Reported	Ireland	People living in Northern Ireland	15
126	Moore, 2002	2002	Not Specified	Cross-sectional	Patient file review	To compare antibiotic resistant strains, particularly fluoroquinolone-resistant organisms, from human clinical sources and chickens originating in Northern Ireland over a similar time period	Disk Diffusion, E-test	Not Reported	Ireland	People living in Northern Ireland	15
127	Uzunovic-Kamberovic, 2009	2009	2002	Cross-sectional	Not specified	To compare the antimicrobial resistance among c. jejuni and c. coli isolated from human infections, retail poultry meat and poultry in Bosnia and Herzegovina	Disk Diffusion	CLSI clinical breakpoints	Bosnia and Herzegovina	Inhabitants of Zenica-Doboj Canton	2491
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130	Campylobacter Sentinel Surveillance Scheme, 2002	2002	04/01/00-05/31/01	Case-control	Survey/Questionnaire	To determine factors affecting the acquisition of a ciprofloxacin-resistant campylobacter jejuni infection	Agar Dilution	h breakpoints for ciprofloxacin at 1 mg/L and erythromycin at 4 mg/L.	United Kingdom	People in the UK with campylobacter	495
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161	Campylobacter Sentinel Surveillance Scheme, 2002	2002	04/01/00-05/31/01	Case-control	Survey/Questionnaire	To determine factors affecting the acquisition of a ciprofloxacin-resistant campylobacter jejuni infection	Agar Dilution	h breakpoints for ciprofloxacin at 1 mg/L and erythromycin at 4 mg/L.	United Kingdom	People in the UK with campylobacter	1884
162	WonHee, 2016	2016	01/--/11-12/--/12	Cross-sectional	Patient file review	To determine the frequency of antimicrobial resistance in a subset of C. jejuni isolates collected in Michigan between 2011 and 2012 and to estimate the genetic diversity of both susceptible and resistant isolates using multilocus sequence typing.	Not Specified	EUCAST clinical breakpoints	United States	People in Michigan with campylobacteriosis	94
163	WonHee, 2016	2016	01/--/11-12/--/12	Cross-sectional	Patient file review	To determine the frequency of antimicrobial resistance in a subset of C. jejuni isolates collected in Michigan between 2011 and 2012 and to estimate the genetic diversity of both susceptible and resistant isolates using multilocus sequence typing.	Not Specified	EUCAST clinical breakpoints	United States	People in Michigan with campylobacteriosis	94
164	WonHee, 2016	2016	01/--/11-12/--/12	Cross-sectional	Patient file review	To determine the frequency of antimicrobial resistance in a subset of C. jejuni isolates collected in Michigan between 2011 and 2012 and to estimate the genetic diversity of both susceptible and resistant isolates using multilocus sequence typing.	Not Specified	EUCAST clinical breakpoints	United States	People in Michigan with campylobacteriosis	94
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167	WonHee, 2016	2016	01/--/11-12/--/12	Cross-sectional	Patient file review	To determine the frequency of antimicrobial resistance in a subset of C. jejuni isolates collected in Michigan between 2011 and 2012 and to estimate the genetic diversity of both susceptible and resistant isolates using multilocus sequence typing.	Not Specified	EUCAST clinical breakpoints	United States	People in Michigan with campylobacteriosis	94
168	van Hees, 2007	2006	2000-2004	Cross-sectional	Patient file review	To describe a nationwide epidemiological analysis of culture-proven Campylobacter infections in The Netherlands during 2000-2004	Not Specified	Not Reported	Netherlands	People of the Netherlands tested for campylobacter during the specified time period	18856
169	van Hees, 2007	2006	2000-2004	Cross-sectional	Patient file review	To describe a nationwide epidemiological analysis of culture-proven Campylobacter infections in The Netherlands during 2000-2004	Not Specified	Not Reported	Netherlands	People of the Netherlands tested for campylobacter during the specified time period	18856
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1	Bottieau, 2011	Norfloxacine-susceptible Campylobacter jejuni	23	Cases of travellers presenting at the participating hospitals with fever after a stay in the tropics or subtropics	Mean age of those with invasive bacterial enteritis was 33 years, range = 11 months-73 years			100	1730 travellers presented with a fever, 594 of those had diarrhoea with their fever, 512 of those had stool examination and cultures, 335 patients were diagnosed with febrile traveller's diarrhoea, invasive bacterial enteritis was confirmed in 114 travellers and suspected in another 36 patients
2	Engberg, 2004	patients from the cohort study with quinolone-sensitive isolates	84	Part of a larger cohort study where isolates were tested . Patients were matched on date of specimen collection and filled in a questionnaire for more information	mean age of 33 (IQR 20-45)	83.3	16.7		Patients were selected from the cohort study based on a resistant campylobacter isolate test, they were followed up with a short questionnaire about illness and fluoroquinolone use, and matched to two randomly selected patients from the cohort study with a sensitive campylobacter isolate. Patients were matched by date of specimen collection. Any unanswered survey question was filled in by info from healthcare providers
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47	Feodoroff, 2010	Campylobacter of domestic origin	40	Patients were identified by presenting with a culture-confirmed campylobacter jejuni infection an filling in a questionnaire about travel	Not specified	59.6	40.4		Patients were identified by presenting with a culture-confirmed campylobacter jejuni infection an filling in a questionnaire about travel
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48	Gallay, 2008	Controls were matched by age to cases as well matched by attending physician	285	a "case" was defined as a resident of metropolitan France who had clinical symptoms of campylobacteriosis and a culture confirmed Campylobacter isolate identified from dates specified. When cases were part of an outbreak, only the first case was enrolled. Controls were selected from the patient registry of the case's physician and matched by age groups and if they were older than 15 they were matched by sex. Potential controls were excluded if they had experienced diarrhea within 1 month before or 1 week after the onset of infection in the matched case or if they were identified >15 days after the date that a Campylobacter isolate was identified with a matched case. If a potential control refused to participate or could not be reached after 5 attempts a search for another control was conducted.	Mean age cases = 19.5, mean age controls = 20		58.2		a "case" was defined as a resident of metropolitan France who had clinical symptoms of campylobacteriosis and a culture confirmed Campylobacter isolate identified from dates specified. When cases were part of an outbreak, only the first case was enrolled. Controls were selected from the patient registry of the case's physician and matched by age groups and if they were older than 15 they were matched by sex. Potential controls were excluded if they had experienced diarrhea within 1 month before or 1 week after the onset of infection in the matched case or if they were identified >15 days after the date that a Campylobacter isolate was identified with a matched case. If a potential control refused to participate or could not be reached after 5 attempts a search for another control was conducted.
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50	Gaudreau, 2003	Men who didn't identify their sexual preference	4	Retrospective chart review followed by isolate testing and susceptibility testing	Age range 26-40		100		Participants were selected and identified by the microbiology lab at the Montreal University's hospital
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53	Gaudreau, 2015	Men who did not indicate that they had had sex with other men	3	Cases were flagged by the university of Montreal's hospital microbiology lab	Age range 21-64		100		Men who were identified as having a lab confirmed campylobacter jejuni infection
54	Gaudreau, 2015	Men who did not indicate that they had had sex with other men	3	Cases were flagged by the university of Montreal's hospital microbiology lab	Age range 21-64		100		Men who were identified as having a lab confirmed campylobacter jejuni infection
55	Gaudreau, 2015	Men who did not indicate that they had had sex with other men	3	Cases were flagged by the university of Montreal's hospital microbiology lab	Age range 21-64		100		Men who were identified as having a lab confirmed campylobacter jejuni infection
56	Gaudreau, 2015	Men who did not indicate that they had had sex with other men	3	Cases were flagged by the university of Montreal's hospital microbiology lab	Age range 21-64		100		Men who were identified as having a lab confirmed campylobacter jejuni infection
57	Ghunaim, 2015	Erythromycin susceptible campylobacter	159	Outpatients with severe and bloody diarrhea are routinely screened at the HMC hospital (Hamad Medical Corporation) for the presence of enteric bacteria using UK standards	34 (age class 1: <1), 44 (age class 2: 1), 31 (age class 3: 2), 43 (age class 4: 3-12), 22 (age class 5: 19-75)	40.2	59.8	0	Those positive for campylobacter and genotyped as well as assessed for sensitivity to each of the four antimicrobials
58	Ghunaim, 2015	Ciprofloxacin susceptible campylobacter	64	Outpatients with severe and bloody diarrhea are routinely screened at the HMC hospital (Hamad Medical Corporation) for the presence of enteric bacteria using UK standards	34 (age class 1: <1), 44 (age class 2: 1), 31 (age class 3: 2), 43 (age class 4: 3-12), 22 (age class 5: 19-75)	40.2	59.8	0	Those positive for campylobacter and genotyped as well as assessed for sensitivity to each of the four antimicrobials
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63	Hakanen, 2003	Those with susceptible C. jejuni who travelled (select a country for comparison)		Travelers returning to Finland from 1995 to 2000 where isolates were collected in two different phases from the laboratory of a large private hospital in Helsinki	Not available	0	0	100	Travelers returning to Finland from 1995 to 2000 with campylobacter jejuni where isolates were collected in two different phases from the laboratory of a large private hospital in Helsinki
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69	Helms, 2005	Campylobacter isolates susceptible to quinolones and/or erythromycin	2506	Cases were identified via a national disease surveillance network for enteric pathogens and cross referenced with the civil registry	Approximately: 27.4 years [range: 0.2-92.3]	0	0	100	All campylobacter isolates collected during the study date period were included, with those with more than one isolate during a period of 6 months only including their first isolate. Susceptibility testing was completed. Information about the patients was collected via a national civil registry
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71	Jenkin, 1998	None		File review	Average age=40, Range=27-53		90		Diarrhea was defined by any notation of diarrhea in the clinical notes by the attending physician

72	Johnson, 2008	ciprofloxacin-susceptible Campylobacter cases	145	Study participants were residents of the Chinook Health Region and Calgary Health Region, aged >16 years, who submitted a stool sample that was positive for the presence of Campylobacter, and who were followed-up by a public health nurse or inspector between 1 February 2004 and 29 July 2005.	Not specified except for over 16 years of age	45.2	54.2	0.5	351 participants were asked to participate, 229 patients consented, 19 censored due to lack of stool sample submission data
73	Johnson, 2008	ciprofloxacin-susceptible Campylobacter cases	145	Study participants were residents of the Chinook Health Region and Calgary Health Region, aged >16 years, who submitted a stool sample that was positive for the presence of Campylobacter, and who were followed-up by a public health nurse or inspector between 1 February 2004 and 29 July 2005.	Not specified except for over 16 years of age	45.2	54.2	0.5	351 participants were asked to participate, 229 patients consented, 19 censored due to lack of stool sample submission data
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81	Koningstein, 2011	Those with a susceptible campylobacter infection and an age group decided upon during analysis	8207	Culture confirmed cases of campylobacter are reported and entered into the National Registry for Enteric Pathogens.	Age is the factor, see results for age breakdowns	0	0	100	Some culture-confirmed campylobacter were sent for susceptibility testing as part of the Danish Integrated Antimicrobial Resistance Monitoring and Research Program (DANMAP) . Personal information was pulled from the Civil Registry System, prior exposure to antimicrobials was determined via the National Prescription Database while education and SES was determined using data from the Integrated Database on Labor Market Research
82	Koningstein, 2011	Those with a susceptible campylobacter infection and an age group decided upon during analysis	10237	Culture confirmed cases of campylobacter are reported and entered into the National Registry for Enteric Pathogens.	Age is the factor, see results for age breakdowns	0	0	100	Some culture-confirmed campylobacter were sent for susceptibility testing as part of the Danish Integrated Antimicrobial Resistance Monitoring and Research Program (DANMAP) . Personal information was pulled from the Civil Registry System, prior exposure to antimicrobials was determined via the National Prescription Database while education and SES was determined using data from the Integrated Database on Labor Market Research
83	Kownhar, 2007	Non-HIV study subjects with Diarrhea	200	Selected based on febrile diarrhea from AIDS specialty hospital, randomly selected based on the inclusion criteria	HIV infected: Average age=37; Non-HIV infected: Average Age=39.3	41.8	58.3	0	Selected from an AIDS specialty hospital in Chennai; Selection criteria for diarrhea were based on the presence of persistent febrile diarrhea for more than 2 days with nausea, headache, and malaise; subjects that were negative for HIV were in the Non-HIV group, while those positive for HIV-1 and diarrhea were in the HIV infected group. Specimens were collected from faecal specimens, strains were from sporadic cases NOT outbreaks
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88	Lu, 2000	Susceptible Campylobacter	0	Retrospective file review	Range=4-81, median=45	42.9	57.1	0	Selected all campylobacter bacteremia files by review of the laboratory records of the University Hospital
89	Nelson, 2004	Persons with ciprofloxacin-susceptible infection	658	Surveillance personnel within the FoodNet sites ascertained all culture-confirmed cases of campylobacter infection within the surveillance area	Median age=34 years, range of <1-96 years	46	54	0	Participants needed to have a culture-confirmed campylobacter infection, completed the FoodNet questionnaire/interview, susceptibility results needed to be available. Those who reported not having diarrhea, who still had diarrhea at the time of interview, and those unable to give an estimated duration if diarrhea were excluded from the main analysis.
90	Nelson, 2004	Persons with ciprofloxacin-susceptible infection	658	Surveillance personnel within the FoodNet sites ascertained all culture-confirmed cases of campylobacter infection within the surveillance area	Median age=34 years, range of <1-96 years	46	54	0	Participants needed to have a culture-confirmed campylobacter infection, completed the FoodNet questionnaire/interview, susceptibility results needed to be available. Those who reported not having diarrhea, who still had diarrhea at the time of interview, and those unable to give an estimated duration if diarrhea were excluded from the main analysis.
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96	Patrick, 2018	Antimicrobial susceptible campylobacter		Participants were identified using FoodNet, a foodborne disease surveillance network in the United States, a subset of which was analyzed for antimicrobial susceptiblity	Median age: 38	45	55	0	Isolates with campylobacter species information
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102	Patrick, 2018	Antimicrobial susceptible campylobacter		Participants were identified using FoodNet, a foodborne disease surveillance network in the United States, a subset of which was analyzed for antimicrobial susceptiblity	Median age: 38	45	55	0	Isolates with campylobacter species information
103	Perlman, 1988	Not applicable		All were seeking care for other medical concerns	Average age=47, Range=39-67	0	100	0	Identified four HIV-infected patients with C.jejuni infection, with persistent or sever infections
104	Ricotta, 2014	Those who are NARMS-linked with a known travel status and identified as traveling non-internationally	3919	Campylobacteriosis cases are captured by FoodNet along with demographics and travel history , viable isolates are routinely sent to CDC NARMS laboratory for susceptibility testing	No international travel average=36.19; international travel average=37.13	45.5	54.5	0	Campylobacteriosis cases are captured by FoodNet along with demographics and travel history , viable isolates are routinely sent to CDC NARMS laboratory for susceptibility testing
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108	Sharma, 2003	Locally-acquired isolates	148	Cases were recruited using voluntary notifications from two participating laboratories of the three major pathology service providers for the population	Not specified	0	0	100	Of the 355 enrolled cases, 240 Campylobacter isolates were detected at the public laboratory. Of these, 171 stored isolates were available for inclusion in this study, of these 155 had travel history information available
109	Sharma, 2003	Locally-acquired isolates	148	Cases were recruited using voluntary notifications from two participating laboratories of the three major pathology service providers for the population	Not specified	0	0	100	Of the 355 enrolled cases, 240 Campylobacter isolates were detected at the public laboratory. Of these, 171 stored isolates were available for inclusion in this study, of these 155 had travel history information available
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111	Sharma, 2003	Locally-acquired isolates	148	Cases were recruited using voluntary notifications from two participating laboratories of the three major pathology service providers for the population	Not specified	0	0	100	Of the 355 enrolled cases, 240 Campylobacter isolates were detected at the public laboratory. Of these, 171 stored isolates were available for inclusion in this study, of these 155 had travel history information available
112	Skjot-Rasmussen, 2009	Domestically acquired human cases		Isolates were obtained from The Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP), travel information was collected by phone interview	Not available	0	0	100	All isolates were susceptibility tested as part of the DANMAP programme.
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113	Skjot-Rasmussen, 2009	Domestically acquired human cases		Isolates were obtained from The Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP), travel information was collected by phone interview	Not available	0	0	100	All isolates were susceptibility tested as part of the DANMAP programme.
114	Skjot-Rasmussen, 2009	Domestically acquired human cases		Isolates were obtained from The Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP), travel information was collected by phone interview	Not available	0	0	100	All isolates were susceptibility tested as part of the DANMAP programme.
115	Smith, 1999	Patients with a sensitive isolate	260	Cases of Campylobacter were reportable to the Minnesota Department of Health Public Health Laboratory. All isolates during 1996 through 1997 were classified as quinolone-resistant or quinolone-sensitive. Each patient with a resistant isolate was matched with two patients with a sensitive isolates.	Not specified	0	0	100	Patients were matched for age (within 10 years), residence (in the seven-county Minneapolis-St.Paul metropolitan area vs. elsewhere in Minnesota), and date of specimen collection. Each patient answered a standardized questionnaire that included questions about clinical history, antimicrobial use, recent diarrheal illness , history of food consumption, animal contact, travel history, and family antimicrobial use.
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125	Moore, 2002	Females and Not determined with a campylobacter infection (ie. Not males)	5	Human clinical isolates were obtained from patients presenting with gastrointestinal symptoms at either a general practitioner or as in patients in hospital.	Range=1-67, Average=29.4	26.7	66.7	6.7	Two hundred human isolates were obtained, isolates were tested for campylobacter and antimicrobial susceptibility.
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127	Uzunovic-Kamberovic, 2009	Age group of those age 0-6	1557	Stool specimens were received from 2,491 consecutive outpatients with sporadic diarrhoea.	1557 aged 0-6, 331 aged 7-14, 204 aged15-19, 311 aged 20-64, 88 aged >64	0	0	100	One isolate per patient was included in the analysis of antibiotic susceptibility, patients of of the Cantonal Public Health Institute in Zenica
128	Uzunovic-Kamberovic, 2009	Age group of those age 0-6	1557	Stool specimens were received from 2,491 consecutive outpatients with sporadic diarrhoea.	1557 aged 0-6, 331 aged 7-14, 204 aged15-19, 311 aged 20-64, 88 aged >64	0	0	100	One isolate per patient was included in the analysis of antibiotic susceptibility, patients of of the Cantonal Public Health Institute in Zenica
129	Campylobacter Sentinel Surveillance Scheme, 2002	People with campylobacter jejuni that is sensitive to ciprofloxacin	148	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
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132	Campylobacter Sentinel Surveillance Scheme, 2002	People with campylobacter jejuni that is sensitive to ciprofloxacin	148	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
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133	Campylobacter Sentinel Surveillance Scheme, 2002	Cases with a sensitive indigenous-acquired campylobacter jejuni infection	1593	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
134	Campylobacter Sentinel Surveillance Scheme, 2002	Cases with a sensitive indigenous-acquired campylobacter jejuni infection	1593	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
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140	Campylobacter Sentinel Surveillance Scheme, 2002	People with campylobacter jejuni that is sensitive to ciprofloxacin	148	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
141	Campylobacter Sentinel Surveillance Scheme, 2002	People with campylobacter jejuni that is sensitive to ciprofloxacin	148	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
142	Campylobacter Sentinel Surveillance Scheme, 2002	People with campylobacter jejuni that is sensitive to ciprofloxacin	148	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
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144	Campylobacter Sentinel Surveillance Scheme, 2002	People with campylobacter jejuni that is sensitive to ciprofloxacin	148	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
145	Campylobacter Sentinel Surveillance Scheme, 2002	People with campylobacter jejuni that is sensitive to ciprofloxacin	148	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
146	Campylobacter Sentinel Surveillance Scheme, 2002	Cases with a sensitive indigenous-acquired campylobacter jejuni infection	1593	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
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149	Campylobacter Sentinel Surveillance Scheme, 2002	Cases with a sensitive indigenous-acquired campylobacter jejuni infection	1593	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
150	Campylobacter Sentinel Surveillance Scheme, 2002	Cases with a sensitive indigenous-acquired campylobacter jejuni infection	1593	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
151	Campylobacter Sentinel Surveillance Scheme, 2002	Cases with a sensitive indigenous-acquired campylobacter jejuni infection	1593	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
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152	Campylobacter Sentinel Surveillance Scheme, 2002	People with campylobacter jejuni that is sensitive to ciprofloxacin	148	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
153	Campylobacter Sentinel Surveillance Scheme, 2002	People with campylobacter jejuni that is sensitive to ciprofloxacin	148	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
154	Campylobacter Sentinel Surveillance Scheme, 2002	People with campylobacter jejuni that is sensitive to ciprofloxacin	148	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
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156	Campylobacter Sentinel Surveillance Scheme, 2002	People with campylobacter jejuni that is sensitive to ciprofloxacin	148	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
157	Campylobacter Sentinel Surveillance Scheme, 2002	Cases with a sensitive indigenous-acquired campylobacter jejuni infection	1593	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
158	Campylobacter Sentinel Surveillance Scheme, 2002	People with campylobacter jejuni that is sensitive to ciprofloxacin	148	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
159	Campylobacter Sentinel Surveillance Scheme, 2002	People with campylobacter jejuni that is sensitive to ciprofloxacin	148	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
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160	Campylobacter Sentinel Surveillance Scheme, 2002	People with campylobacter jejuni that is sensitive to ciprofloxacin	148	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
161	Campylobacter Sentinel Surveillance Scheme, 2002	Cases with a sensitive indigenous-acquired campylobacter jejuni infection	1593	Campylobacter isolates were referred from Public Health Laboratory Service and the National Health Service laboratories within the sentinel surveillance catchment area	cases mean age=39, control mean age=38	52.3	47.7	0	Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Daily water consumption was coded to differentiate no exposure from one to four, five to nine and >10 glasses of water drunk. Patient age was arranged in 10 year age groups. Individuals with missing data were omitted from the analyses using those data.
162	WonHee, 2016	Susceptible Ccampylobacter jejuni	30	C. jejuni isolates were obtained from patients with campylobacteriosis identified via the Michigan State University Enteric Research Investigative Network surveillance system	21 (<=2), 25 (3-23), 24 (24-50), 24 (>50)	42.9	57.1	0	Isolates were recovered from patients with campylobacteriosis in participating surveillance hospitals in Michigan between the specified dates.
163	WonHee, 2016	Susceptible Ccampylobacter jejuni	30	C. jejuni isolates were obtained from patients with campylobacteriosis identified via the Michigan State University Enteric Research Investigative Network surveillance system	21 (<=2), 25 (3-23), 24 (24-50), 24 (>50)	42.9	57.1	0	Isolates were recovered from patients with campylobacteriosis in participating surveillance hospitals in Michigan between the specified dates.
Factor ID	Paper REF	What is the comparison group?	What is the sample size of the comparison group?	How was the population/participants identified?	What are the age details for the total sample? (eg. average age, range, etc.)	What were the proportion of females included in the study?	What were the proportion of males included in the study?	What were the proportion of not specifed gender in the study?	What were the participant selection methods?

164	WonHee, 2016	Susceptible Ccampylobacter jejuni	30	C. jejuni isolates were obtained from patients with campylobacteriosis identified via the Michigan State University Enteric Research Investigative Network surveillance system	21 (<=2), 25 (3-23), 24 (24-50), 24 (>50)	42.9	57.1	0	Isolates were recovered from patients with campylobacteriosis in participating surveillance hospitals in Michigan between the specified dates.
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167	WonHee, 2016	Susceptible Ccampylobacter jejuni	30	C. jejuni isolates were obtained from patients with campylobacteriosis identified via the Michigan State University Enteric Research Investigative Network surveillance system	21 (<=2), 25 (3-23), 24 (24-50), 24 (>50)	42.9	57.1	0	Isolates were recovered from patients with campylobacteriosis in participating surveillance hospitals in Michigan between the specified dates.
168	van Hees, 2007	Endemic-related Campylobacter infection	17156	Patients were identified by isolates sent to the National Institute for Public Health and the Environment in the Netherlands and their Infectious Disease Surveillance Information System network of sentinel laboratories.	Not specified	0	0	100	Those in the Laboratory Surveillance system (LSI) had travel-related information collected
Factor ID	Paper REF	What is the comparison group?	What is the sample size of the comparison group?	How was the population/participants identified?	What are the age details for the total sample? (eg. average age, range, etc.)	What were the proportion of females included in the study?	What were the proportion of males included in the study?	What were the proportion of not specifed gender in the study?	What were the participant selection methods?

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Factor ID	Paper REF	Number of factors investigated?	Definition of the factor:	What is the sample size of the exposed group?	Location	Sub-location	Campylobacter species	What types of infection are reported in the study?	Specify the type of resistant infection	Type of analysis	Type of Result:
1	Bottieau, 2011	1	Susceptible vs norfloxacine resistant campylobacter jejuni in patients per travel destination	49	Table (specify number)	2	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Not specified	Count
2	Engberg, 2004	10	Beef (not cold cuts)	100	Table (specify number)	3	Jejuni	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression	Odds Ratio
3	Engberg, 2004	10	Fresh chicken consumption	72	Table (specify number)	3	Jejuni	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression	Odds Ratio
4	Engberg, 2004	10	Fresh poultry other than chicken and turkey	14	Table (specify number)	3	Jejuni	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression	Odds Ratio
5	Engberg, 2004	10	Sausages	41	Table (specify number)	3	Jejuni	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression	Odds Ratio
6	Engberg, 2004	10	Handling of raw meat	52	Table (specify number)	3	Jejuni	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression	Odds Ratio
7	Engberg, 2004	10	Travel abroad within the last 7 days	42	Table (specify number)	3	Jejuni	Not specified	Quinolones (eg. Nalidixic acid)	Univariate Linear Regression; Multivariate Regression	Odds Ratio
8	Engberg, 2004	10	Animal contact	59	Table (specify number)	3	Jejuni	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression	Odds Ratio
9	Engberg, 2004	10	Fluoroquinolone treatment after illness onset but before stool sample or 4 weeks before symptom onset	13	Table (specify number)	3	Jejuni	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression	Odds Ratio
10	Engberg, 2004	10	Public water supply	85	Table (specify number)	3	Jejuni	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression	Odds Ratio
11	Engberg, 2004	10	Swimming (pool, ocean, lake, or other place)	36	Table (specify number)	3	Jejuni	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression	Odds Ratio
12	Evans, 2009	15	Food History 1: Eating away from home		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
13	Evans, 2009	15	Food history 2: any chicken		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
14	Evans, 2009	15	Food history 3: any pork		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
15	Evans, 2009	15	Food history 4: any lamb or mutton		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
16	Evans, 2009	15	Food history 5: Any unpasteurized milk		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
17	Evans, 2009	15	Handled raw chicken		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
18	Evans, 2009	15	Store raw chicken in fridge		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
19	Evans, 2009	15	Travel-related infection 4: ate chicken abroad	74	Table (specify number)	2	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
20	Evans, 2009	15	Travel-related infection 5: Ate eggs abroad	74	Table (specify number)	2	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
21	Evans, 2009	15	Domestically-acquired infection 4: ate chicken in the UK	71	Table (specify number)	2	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count

Factor ID	Paper REF	Number of factors investigated?	Definition of the factor:	What is the sample size of the exposed group?	Location	Sub-location	Campylobacter species	What types of infection are reported in the study?	Specify the type of resistant infection	Type of analysis	Type of Result:
22	Evans, 2009	15	Domestically-acquired infection 5: ate pre-cooked cold meats in the UK	71	Table (specify number)	2	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
23	Evans, 2009	15	Travel abroad in last 7 days		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
24	Evans, 2009	15	Travel-related infection 1: ill household contact	74	Table (specify number)	2	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
25	Evans, 2009	15	Travel-related infection 2: Spain (versus other countries)	74	Table (specify number)	2	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
26	Evans, 2009	15	Travel-related infection vs domestically acquired infection (factor was not specifically compared in the text but could be compared with analysis)	71	Table (specify number)	2	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
27	Evans, 2009	15	Age group 1/3: 18-44 vs <18 years	145	Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
28	Evans, 2009	15	Age Group 2 = 45-64 vs <18		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
29	Evans, 2009	15	Domestically acquired infection 1: Student	71	Table (specify number)	2	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
30	Evans, 2009	15	Employment status 2 [Student vs *assumed* unemployed]		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
31	Evans, 2009	15	Living with a child under 5 years (vs not)		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
32	Evans, 2009	15	Domestically acquired infection 2: living with child under 5 years	71	Table (specify number)	2	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
33	Evans, 2009	15	Gender [Male vs other for cipR patients (n=145) vs cipS patietns (n=411)]	145	Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
34	Evans, 2009	15	Employment Status 1: Employed (assumed it's vs. unemployed)		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
35	Evans, 2009	15	Age Group 3: 65+ vs <18		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
36	Evans, 2009	15	Own any pets		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
37	Evans, 2009	15	Contact with zoo animals		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
38	Evans, 2009	15	Domestically-acquired infection 6: own rabbit or guinea pig	71	Table (specify number)	2	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count

Factor ID	Paper REF	Number of factors investigated?	Definition of the factor:	What is the sample size of the exposed group?	Location	Sub-location	Campylobacter species	What types of infection are reported in the study?	Specify the type of resistant infection	Type of analysis	Type of Result:
39	Evans, 2009	15	Antibiotic use in the previous month		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
40	Evans, 2009	15	Diabetic (vs. not)		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
41	Evans, 2009	15	Antacid use in the previous month		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
42	Evans, 2009	15	Food history 6: Any tap water		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
43	Evans, 2009	15	Food history 7: Any still bottled wateer		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
44	Evans, 2009	15	Food history 8: Any sparkling bottled water		Table (specify number)	1	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
45	Evans, 2009	15	Travel-related infection 3: Drank still bottled water abroad	74	Table (specify number)	2	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
46	Evans, 2009	15	Domestically-acquired infection 3: drank sparkling bottled water in the UK	71	Table (specify number)	2	Not specified	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression; Logistic Regression	Count
47	Feodoroff, 2010	1	Travel-related vs domestic acquired infection	126	Text (specify location)	P3, Results	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Not specified	Qualitative
48	Gallay, 2008	1	Association between use of antibiotics in the month before disease onset and ciprofloxacin-resistant Campylobacter infection in a case-control study by species: ALL SPECIES	60	Table (specify number)	4	Jejuni, coli, fetus, lari	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Not specified	Count
49	Gallay, 2008	1	Association between use of antibiotics in the month before disease onset and ciprofloxacin-resistant Campylobacter infection: C.JEJUNI ONLY	42	Table (specify number)	4	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Not specified	Count
50	Gaudreau, 2003	1	Men who have sex with men (MSM)	10	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Macrolides (eg. Erythromycin, azithromycin)	Not specified	Count
51	Gaudreau, 2003	1	Men who have sex with men (MSM)	10	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Tetracyclines (eg. Tetracycline)	Not specified	Count
52	Gaudreau, 2003	1	Men who have sex with men (MSM)	10	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Not specified	Count
53	Gaudreau, 2015	1	Men who have sex with men	28	Text (specify location)	Page 3, last paragraph of the results	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Not specified	Count
54	Gaudreau, 2015	1	Men who have sex with men	28	Text (specify location)	Page 3, last paragraph of the results	Jejuni	Gastrointestinal tract infection	Quinolones (eg. Nalidixic acid)	Not specified	Count

Factor ID	Paper REF	Number of factors investigated?	Definition of the factor:	What is the sample size of the exposed group?	Location	Sub-location	Campylobacter species	What types of infection are reported in the study?	Specify the type of resistant infection	Type of analysis	Type of Result:
55	Gaudreau, 2015	1	Men who have sex with men	28	Text (specify location)	Page 3, last paragraph of the results	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Not specified	Count
56	Gaudreau, 2015	1	Men who have sex with men	28	Text (specify location)	Page 3, last paragraph of the results	Jejuni	Gastrointestinal tract infection	Tetracyclines (eg. Tetracycline)	Not specified	Count
57	Ghunaim, 2015	3	Country of origin		Table (specify number)	2	Jejuni	Gastrointestinal tract infection	Macrolides (eg. Erythromycin, azithromycin)	Univariate Linear Regression	Proportion (%)
58	Ghunaim, 2015	3	Country of origin		Table (specify number)	2	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Proportion (%)
59	Ghunaim, 2015	3	Gender: Male vs Female	110	Table (specify number)	2	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Proportion (%)
60	Ghunaim, 2015	3	Gender: Male vs Female	15	Table (specify number)	2	Jejuni	Gastrointestinal tract infection	Macrolides (eg. Erythromycin, azithromycin)	Univariate Linear Regression	Proportion (%)
61	Ghunaim, 2015	3	Age class		Table (specify number)	2	Jejuni	Gastrointestinal tract infection	Macrolides (eg. Erythromycin, azithromycin)	Univariate Linear Regression	Proportion (%)
62	Ghunaim, 2015	3	Age class		Table (specify number)	2	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Proportion (%)
63	Hakanen, 2003	6	Travel to Spain (including the Canary Islands)	77	Table (specify number)	2	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
64	Hakanen, 2003	6	Travel to Thailand	50	Table (specify number)	2	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
65	Hakanen, 2003	6	Travel to India	23	Table (specify number)	2	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
66	Hakanen, 2003	6	Travel to China	12	Table (specify number)	2	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
67	Hakanen, 2003	6	Travel to Portugal	11	Table (specify number)	2	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
68	Hakanen, 2003	6	Difference between two study periods: 1995-1997 (comparison group) compared to 1998-2000 (exposed group)	149	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Multiple Linear Regression	Count
69	Helms, 2005	1	Domestically acquired infection vs Travel acquired infection [two different drug classes explored]	554	Text (specify location)	p1052, Results	Not specified	Gastrointestinal tract infection	Quinolones (eg. Nalidixic acid)	Not specified	Count
70	Helms, 2005	1	Domestically acquired infection vs Travel acquired infection [two different drug classes explored]	554	Text (specify location)	p1052, Results	Not specified	Gastrointestinal tract infection	Macrolides (eg. Erythromycin, azithromycin)	Not specified	Count
71	Jenkin, 1998				Table (specify number)	1	Upsaliensis	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Not specified	Other, specify

Factor ID	Paper REF	Number of factors investigated?	Definition of the factor:	What is the sample size of the exposed group?	Location	Sub-location	Campylobacter species	What types of infection are reported in the study?	Specify the type of resistant infection	Type of analysis	Type of Result:
72	Johnson, 2008	7	Foreign travel-related infection: Symptoms started at least 2 days after the first day of travel outside the United States and Canada and within 3 days of returning [yes/no] Macro-region of infection source country: broken down by Latin America, Asia, Europe		Text (specify location)	Pg. 909, Discussion para 2	Jejuni, coli, undetermined	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Not specified	Other, specify
73	Johnson, 2008	7	Sex: Female vs Male	209	Table (specify number)	2	Jejuni, coli, undetermined	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Logistic Regression	Proportion (%)
74	Johnson, 2008	7	Age, 4 categories= <28, 28-37, 38-49, 50+		Table (specify number)	2	Jejuni, coli, undetermined	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Logistic Regression	Proportion (%)
75	Johnson, 2008	7	College or university education		Table (specify number)	2	Jejuni, coli, undetermined	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Logistic Regression	Proportion (%)
76	Johnson, 2008	7	Season of reported infection		Table (specify number)	2	Jejuni, coli, undetermined	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Logistic Regression	Proportion (%)
77	Johnson, 2008	7	Health region		Table (specify number)	2	Jejuni, coli, undetermined	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Logistic Regression	Proportion (%)
78	Johnson, 2008	7	Rural residence		Table (specify number)	2	Jejuni, coli, undetermined	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Logistic Regression	Proportion (%)
79	Johnson, 2008	7	Species: C.jejuni		Table (specify number)	2	Jejuni, coli, undetermined	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Logistic Regression	Proportion (%)
80	Johnson, 2008	7	Possession of non-prescribed antibiotics: participant possess antibiotics that were not prescribed for them that were saved for future use		Text (specify location)	Page 909, Discussion para 5	Jejuni, coli, undetermined	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Not specified	Other, specify
81	Koningstein, 2011	2	Age group by class of drug	2268	Table (specify number)	2	Not specified	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Not specified	Count
82	Koningstein, 2011	2	Age group by drug class	238	Table (specify number)	2	Not specified	Gastrointestinal tract infection	Macrolides (eg. Erythromycin, azithromycin)	Not specified	Count
83	Kownhar, 2007	1	HIV (n=16) vs Non-HIV (n=5) [11 antibiotics tested]	16	Table (specify number)	2	Jejuni	Gastrointestinal tract infection	Quinolones (eg. Nalidixic acid)	Not specified	Count
84	Kownhar, 2007	1	HIV (n=16) vs Non-HIV (n=5) [11 antibiotics tested]	16	Table (specify number)	2	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Not specified	
85	Kownhar, 2007	1	HIV (n=16) vs Non-HIV (n=5) [11 antibiotics tested]	16	Table (specify number)	2	Jejuni	Gastrointestinal tract infection	Macrolides (eg. Erythromycin, azithromycin)	Not specified	
86	Kownhar, 2007	1	HIV (n=16) vs Non-HIV (n=5) [11 antibiotics tested]	16	Table (specify number)	2	Jejuni	Gastrointestinal tract infection	Quinolones (eg. Nalidixic acid)	Not specified	
87	Kownhar, 2007	1	HIV (n=16) vs Non-HIV (n=5) [11 antibiotics tested]	16	Table (specify number)	2	Jejuni	Gastrointestinal tract infection	Tetracyclines (eg. Tetracycline)	Not specified	

Factor ID	Paper REF	Number of factors investigated?	Definition of the factor:	What is the sample size of the exposed group?	Location	Sub-location	Campylobacter species	What types of infection are reported in the study?	Specify the type of resistant infection	Type of analysis	Type of Result:
88	Lu, 2000	1	Appropriate vs inappropriate antimicrobial agents	10	Text (specify location)	Page 615, paragraph 3	Jejuni, coli	Blood-stream infection	Macrolides (eg. Erythromycin, azithromycin)	Not specified	Count
89	Nelson, 2004	7	Foreign travel: yes vs no	77	Table (specify number)	1	Not specified	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Fisher's exact test	Count
90	Nelson, 2004	7	Race: White vs other	653	Table (specify number)	1	Not specified	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Fisher's exact test	Count
91	Nelson, 2004	7	Sex: Male vs other	395	Table (specify number)	1	Not specified	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Fisher's exact test	Count
92	Nelson, 2004	7	Residence: Urban/Suburban vs other	500	Table (specify number)	1	Not specified	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Fisher's exact test	Count
93	Nelson, 2004	7	Education: Bachelor's degree or higher vs other	312	Table (specify number)	1	Not specified	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Fisher's exact test	Count
94	Nelson, 2004	7	Household income: >60,000 vs lower	260	Table (specify number)	1	Not specified	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Fisher's exact test	Count
95	Nelson, 2004	7	Pre-existing medical condition: yes vs no	29	Table (specify number)	1	Not specified	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Fisher's exact test	Count
96	Patrick, 2018	5	International Travel	6010	Text (specify location)	Pg.4, Results	Jejuni	Both		Not specified	Odds Ratio
97	Patrick, 2018	5	International travel	665	Text (specify location)	Pg.4, Results	Jejuni, Coli	Both		Not specified	Odds Ratio
98	Patrick, 2018	5	Age: Over vs under 20	6010	Text (specify location)	Pg.4, Results	Jejuni	Both		Not specified	Odds Ratio
99	Patrick, 2018	5	Race: Asian vs other	6010	Text (specify location)	Pg.4, Results	Jejuni	Both		Not specified	Odds Ratio
100	Patrick, 2018	5	Metro vs suburban and rural areas	6010	Text (specify location)	Pg.4, Results	Jejuni	Both		Not specified	Count
101	Patrick, 2018	5	Campylobacter species		Text (specify location)	Pg.4, Results	Jejuni, Coli	Both	Quinolones (eg. Nalidixic acid)	Not specified	Proportion (%)
102	Patrick, 2018	5			Text (specify location)	Pg.4, Results	Jejuni, Coli	Both	Macrolides (eg. Erythromycin, azithromycin)	Not specified	Proportion (%)
103	Perlman, 1988	1	Erythromycin use and HIV	4	Text (specify location)	p.542, Results para 1	Jejuni, Coli	Gastrointestinal tract infection	Macrolides (eg. Erythromycin, azithromycin)	Not specified	Other, specify
104	Ricotta, 2014	3	Single destination international travel vs Multi/unknown destination international travel vs non-international travel	885	Other, specify	Figure 1	Mostly jejuni	Gastrointestinal tract infection	Quinolones (eg. Nalidixic acid)	Not specified	Count
105	Ricotta, 2014	3	Multi/unknown destination international travel vs single destination international travel vs non-international travel	3919	Other, specify	Figure 1	Mostly jejuni	Gastrointestinal tract infection	Macrolides (eg. Erythromycin, azithromycin)	Not specified	Count
106	Ricotta, 2014	3	Resistance based on travel to single destination		Table (specify number)	2	Mostly jejuni	Gastrointestinal tract infection	Quinolones (eg. Nalidixic acid)	Not specified	Count

Factor ID	Paper REF	Number of factors investigated?	Definition of the factor:	What is the sample size of the exposed group?	Location	Sub-location	Campylobacter species	What types of infection are reported in the study?	Specify the type of resistant infection	Type of analysis	Type of Result:
107	Ricotta, 2014	3	Macrolide Resistant Isolates based on single destination travel		Table (specify number)	2	Mostly jejuni	Gastrointestinal tract infection	Macrolides (eg. Erythromycin, azithromycin)	Not specified	Count
108	Sharma, 2003	1	Locally-acquired vs overseas-acquired by antibiotic	7	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Proportion (%)
109	Sharma, 2003	1	Locally-acquired vs overseas-acquired by antibiotic	7	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Tetracyclines (eg. Tetracycline)	Univariate Linear Regression	Proportion (%)
110	Sharma, 2003	1	Locally-acquired vs overseas-acquired by antibiotic	7	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Macrolides (eg. Erythromycin, azithromycin)	Univariate Linear Regression	Proportion (%)
111	Sharma, 2003	1	Locally-acquired vs overseas-acquired by antibiotic	7	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Quinolones (eg. Nalidixic acid)	Univariate Linear Regression	Proportion (%)
112	Skjot-Rasmussen, 2009	1	Travel associated human cases vs domestically acquired human cases in 2006 and 2007	120	Other, specify	Figure 1	Jejuni	Not specified	Macrolides (eg. Erythromycin, azithromycin)	Not specified	Proportion (%)
113	Skjot-Rasmussen, 2009	1	Travel associated human cases vs domestically acquired human cases in 2006 and 2007	120	Other, specify	Figure 1	Jejuni	Not specified	Tetracyclines (eg. Tetracycline)	Not specified	Proportion (%)
114	Skjot-Rasmussen, 2009	1	Travel associated human cases vs domestically acquired human cases in 2006 and 2007	120	Other, specify	Figure 1	Jejuni	Not specified	Quinolones (eg. Nalidixic acid)	Not specified	Proportion (%)
115	Smith, 1999	9	Foreign Travel: Overall	130	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Quinolones (eg. Nalidixic acid)	Univariate Linear Regression; Multivariate Regression	Count
116	Smith, 1999	9	Foreign Travel: to Mexico	130	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Quinolones (eg. Nalidixic acid)	Univariate Linear Regression; Multivariate Regression	Count
117	Smith, 1999	9	Foreign Travel: To Caribbean countries, South America, or Central America (not Mexico)	130	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Quinolones (eg. Nalidixic acid)	Univariate Linear Regression; Multivariate Regression	Count
118	Smith, 1999	9	Travel within the United States outside of Minnesota	130	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Quinolones (eg. Nalidixic acid)	Univariate Linear Regression; Multivariate Regression	Count
119	Smith, 1999	9	Foreign Travel: to Asia	130	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Quinolones (eg. Nalidixic acid)	Univariate Linear Regression; Multivariate Regression	Count
120	Smith, 1999	9	Foreign Travel: to Spain	130	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Quinolones (eg. Nalidixic acid)	Univariate Linear Regression; Multivariate Regression	Count
121	Smith, 1999	9	Contact with pets	130	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Quinolones (eg. Nalidixic acid)	Univariate Linear Regression; Multivariate Regression	Count
122	Smith, 1999	9	Use of a quinolone before the collection of stool specimens	130	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Quinolones (eg. Nalidixic acid)	Univariate Linear Regression; Multivariate Regression	Count
123	Smith, 1999	9	Drinking untreated water	130	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Quinolones (eg. Nalidixic acid)	Univariate Linear Regression; Multivariate Regression	Count
124	Smith, 1999	9	Swimming	130	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Quinolones (eg. Nalidixic acid)	Univariate Linear Regression; Multivariate Regression	Count

Factor ID	Paper REF	Number of factors investigated?	Definition of the factor:	What is the sample size of the exposed group?	Location	Sub-location	Campylobacter species	What types of infection are reported in the study?	Specify the type of resistant infection	Type of analysis	Type of Result:
125	Moore, 2002	1	Gender/Sex: Male vs not male	10	Table (specify number)	5	15 jejuni, 2 coli	Gastrointestinal tract infection	Tetracyclines (eg. Tetracycline)	Not specified	Rate
126	Moore, 2002	1	Gender/Sex: Male vs not male	10	Table (specify number)	5	15 jejuni, 2 coli	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Not specified	Count
127	Uzunovic-Kamberovic, 2009	1	Age group of 20-64 compared to the age group of 0-6	311	Text (specify location)	P.177, Paragraph 1	Jejuni and Coli	Gastrointestinal tract infection	Macrolides (eg. Erythromycin, azithromycin)	Not specified	Proportion (%)
128	Uzunovic-Kamberovic, 2009	1	Age group of 20-64 compared to the age group of 0-6	311	Text (specify location)	P.177, Paragraph 1	Jejuni and Coli	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Not specified	Proportion (%)
129	Campylobacter Sentinel Surveillance Scheme, 2002	18	Consumption of chicken	347	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
130	Campylobacter Sentinel Surveillance Scheme, 2002	18	Consumption of sausage	347	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
131	Campylobacter Sentinel Surveillance Scheme, 2002	18	Consumption of mains water	347	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
132	Campylobacter Sentinel Surveillance Scheme, 2002	18	Consumption of baby food	347	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
133	Campylobacter Sentinel Surveillance Scheme, 2002	15	Indigenous acquired: Cold meats (pre-cooked)	291	Table (specify number)	3	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
134	Campylobacter Sentinel Surveillance Scheme, 2002	15	Indigenous acquired: Pate	291	Table (specify number)	3	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
135	Campylobacter Sentinel Surveillance Scheme, 2002	15	Indigenous acquired: Organic vegetables	291	Table (specify number)	3	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
136	Campylobacter Sentinel Surveillance Scheme, 2002	15	Indigenous acquired: Fish and shellfish	291	Table (specify number)	3	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
137	Campylobacter Sentinel Surveillance Scheme, 2002	15	Indigenous acquired: Eating in restaurants	291	Table (specify number)	3	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
138	Campylobacter Sentinel Surveillance Scheme, 2002	15	Indigenous acquired: Barbequed food	291	Table (specify number)	3	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count

Factor ID	Paper REF	Number of factors investigated?	Definition of the factor:	What is the sample size of the exposed group?	Location	Sub-location	Campylobacter species	What types of infection are reported in the study?	Specify the type of resistant infection	Type of analysis	Type of Result:
139	Campylobacter Sentinel Surveillance Scheme, 2002	15	Indigenous acquired: Baby food	291	Table (specify number)	3	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
140	Campylobacter Sentinel Surveillance Scheme, 2002	18	Travel to spain (versus other countries)	347	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
141	Campylobacter Sentinel Surveillance Scheme, 2002	18	Cyprus (versus other countries)	347	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
142	Campylobacter Sentinel Surveillance Scheme, 2002	18	Portugal (versus other countries)	347	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
143	Campylobacter Sentinel Surveillance Scheme, 2002	18	Turkey (versus other countries)	347	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
144	Campylobacter Sentinel Surveillance Scheme, 2002	18	France (versus other countries)	347	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
145	Campylobacter Sentinel Surveillance Scheme, 2002	18	Africa (versus other countries)	347	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
146	Campylobacter Sentinel Surveillance Scheme, 2002	15	Indigenous acquired: Summer (versus other seasons)	291	Table (specify number)	3	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
147	Campylobacter Sentinel Surveillance Scheme, 2002	15	Indigenous acquired: School children	291	Table (specify number)	3	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
148	Campylobacter Sentinel Surveillance Scheme, 2002	15	Indigenous acquired: Semi-skilled manual workers	291	Table (specify number)	3	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
149	Campylobacter Sentinel Surveillance Scheme, 2002	15	Indigenous acquired: Retired individuals	291	Table (specify number)	3	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
150	Campylobacter Sentinel Surveillance Scheme, 2002	15	Indigenous acquired: Autumn (versus other seasons)	291	Table (specify number)	3	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
151	Campylobacter Sentinel Surveillance Scheme, 2002	15	Indigenous acquired: Winter (versus other seasons)	291	Table (specify number)	3	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count

Factor ID	Paper REF	Number of factors investigated?	Definition of the factor:	What is the sample size of the exposed group?	Location	Sub-location	Campylobacter species	What types of infection are reported in the study?	Specify the type of resistant infection	Type of analysis	Type of Result:
152	Campylobacter Sentinel Surveillance Scheme, 2002	18	Contact with animals	347	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
153	Campylobacter Sentinel Surveillance Scheme, 2002	18	Contact with a pet dog	347	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
154	Campylobacter Sentinel Surveillance Scheme, 2002	18	Contact with a pet bird	347	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
155	Campylobacter Sentinel Surveillance Scheme, 2002	18	Contact with a pet rodent	347	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
156	Campylobacter Sentinel Surveillance Scheme, 2002	18	Contact with a pet hamster	347	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
157	Campylobacter Sentinel Surveillance Scheme, 2002	15	Indigenous acquired: Contact with a pet guinea pig	291	Table (specify number)	3	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
158	Campylobacter Sentinel Surveillance Scheme, 2002	18	Consumption of bottled water	347	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
159	Campylobacter Sentinel Surveillance Scheme, 2002	18	Consumption of filtered jug water	347	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
160	Campylobacter Sentinel Surveillance Scheme, 2002	18	Swimming	347	Table (specify number)	1	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
161	Campylobacter Sentinel Surveillance Scheme, 2002	15	Indigenous acquired: Private water supplies	291	Table (specify number)	3	Jejuni	Gastrointestinal tract infection	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression	Count
162	WonHee, 2016	6	Home prepared chicken	18	Table (specify number)	3	Jejuni	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression	Odds Ratio
163	WonHee, 2016	6	Foreign travel	18	Table (specify number)	3	Jejuni	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression	Odds Ratio
164	WonHee, 2016	6	Sex (Female)	18	Table (specify number)	3	Jejuni	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression	Odds Ratio
165	WonHee, 2016	6	Season (winter)	18	Table (specify number)	3	Jejuni	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression	Odds Ratio
166	WonHee, 2016	6	Age (years)	18	Table (specify number)	3	Jejuni	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression	Odds Ratio
167	WonHee, 2016	6	Domestic animal contact	18	Table (specify number)	3	Jejuni	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Univariate Linear Regression; Multivariate Regression	Odds Ratio
168	van Hees, 2007	4	Endemic vs travel-related Campylobacter infection	1700	Table (specify number)	2	94% jejuni	Not specified	Fluoroquinolones (eg. Ciprofloxacin)	Not specified	Count

Factor ID	Paper REF	Number of factors investigated?	Definition of the factor:	What is the sample size of the exposed group?	Location	Sub-location	Campylobacter species	What types of infection are reported in the study?	Specify the type of resistant infection	Type of analysis	Type of Result:
169	van Hees, 2007		Qualitative trends		Text (specify location)	p.306-308	94% jejuni	Not specified	Tetracyclines (eg. Tetracycline)	Not specified	Count
170	van Hees, 2007						94% jejuni	Not specified	Macrolides (eg. Erythromycin, azithromycin)	Not specified	Count

Factor ID	Paper REF	Result and variation	Statistical Significance (p-value):	Please provide any additional information about the factors below (Including if there is discussion about WGS)	If needed, notes about paper in general, including critical appraisal of article
1	Bottieau, 2011	Sub-saharan Africa=5/16 resistant, Southern Asia14/23 resistant, North Africa-Middle East=5/6 resistant, Latin America=2/4 resistant			
2	Engberg, 2004	27/42 patients with resistant isolates, 73/84 patients with sensitive isolates; Univariate [matched OR 0.31, 95%CI=0.13 to 0.73, p=0.008], Multivariate [N/A]			
3	Engberg, 2004	14/42 patients with resistant isolates, 58/84 patients with sensitive isolates; Univariate [matched OR=0.17, 95%CI=0.06 to 0.45, p=0.0004] Multivariate [matched OR = 0.04, 95%CI=0.004 to 0.39, p=0.005]			
4	Engberg, 2004	7/42 patients with resistant isolates, 7/84 patients with sensitive isolates; Univariate [matched OR=2.40, 95%CI=0.73 to 7.86, p=0.148] Multivariate [matched OR=19.10, 95%CI=2.18 to 167.30, p=0.008]			
5	Engberg, 2004	8/42 patients with resistant isolates, 33/84 patients with sensitive isolates; Univariate [matched OR=0.32, 95%CI=0.12 to 0.88, p=0.027], Multivariate [N/A]			
6	Engberg, 2004	9/42 patients with resistant isolates 43/84 patients with resistant isolates; Univariate [matched OR=0.14, 95%CI=0.04 to 0.48, p=0.002] Multivariate [N/A]			
7	Engberg, 2004	30/42 patients with resistant isolates; 12/84 patients with sensitive isolates Univariate [matched OR 12.12, 95%CI=4.23 to 34.73, p<0.0001] Multivariate [matched OR 16.81, 95%CI=3.44 to 82.20, p=0.001]			
8	Engberg, 2004	14/42 patients with resistant isolates 45/84 patients with sensitive isolates; Univariate [matched OR=0.44, 95%CI=0.20 to 0.94, p=0.032] Multivariate [N/A]			
9	Engberg, 2004	8/42 patients with resistant isolates, 5/84 patients with sensistive isolates; Univariate [matched OR 4.44, 95% CI=1.15 to 17.09, p=0.031] Multivariate [N/A]			
10	Engberg, 2004	19/42 patients with resistant isolates 66/84 patients with sensitive isolates; Univariate [matched OR=0.17, 95%CI=0.06 to 0.46, p=0.001] Multivariate [N/A]			
11	Engberg, 2004	20/42 patients with resistant isolates 16/84 patients with sensitive isolates; Univariate [matched OR=3.22, 95%CI=1.48 to 7.00, p=0.003] Multivariate [matched OR=5.01, 95%CI=1.14 to 21.99, p=0.033]			
12	Evans, 2009	Resistant=91/141, Susceptible=297/406, Crude OR (95% CI)=0.7 (0.4-1.0), p=0.07			
13	Evans, 2009	Resistant= 128/144, Susceptible=364/410, Crude OR (95% CI)=1.0 (0.5-2.0), p=0.91			

Factor ID	Paper REF	Result and variation	Statistical Significance (p-value):	Please provide any additional information about the factors below (Including if there is discussion about WGS)	If needed, notes about paper in general, including critical appraisal of article
14	Evans, 2009	Resistant=58/142, Susceptible=181/407, Crude OR (95%CI)=0.9 (0.6-1.3), p=0.05			
15	Evans, 2009	Resistant=65/142, Susceptible=149/405, Crude OR (95% CI)=1.5 (1.0-2.2), p=0.07			
16	Evans, 2009	Resistant=2/99, Susceptible=9/390, Crude OR (95% CI)=0.9 (0.0-4.5), p=1.00			
17	Evans, 2009	Resistant=47/104, Susceptible=168/393, Crude OR (95% CI)=1.1(0.7-1.8), p=0.74			
18	Evans, 2009	Resistant=35/141, Susceptible=176/404, Crude OR (95% CI)=0.4(0.3-0.7), p<0.001			
19	Evans, 2009	Resistant=66/74, Susceptible=17/22, Crude OR (95% CI)=2.4 (0.6-9.7), p=0.17			
20	Evans, 2009	Resistant=57/74, Susceptible=13/23, Crude OR (95%CI)=2/6 (0.9-7.7), p=0.099			
21	Evans, 2009	Resistant=59/70, Susceptible=344/387, Crude OR (95% CI)=0.7 (0.3-1.5), p=0.37			
22	Evans, 2009	Resistant=55/69, Susceptible=305/384, Crude OR (95% CI)=1.0 (0.5-2.1), p=0.91			
23	Evans, 2009	Resistant=74/145, Susceptible=24/411, Crude OR (95%CI)=16.8 (9.7-29.6), p<0.001, Adjusted OR (95% CI)=24 (12.6-45.9), adjusted p<0.001			
24	Evans, 2009	Resistant=6/74, Susceptible=4/24, Crude OR (95% CI)=0.2(0.0-0.7), p=0.01, Adjusted OR=0.2(0.0-0.6), Adjusted p=0.009			
25	Evans, 2009	Resistant=36/74, Susceptible=6/24, Crude OR (95% CI)=2.8 (0.9-9.7), p=0.07			
26	Evans, 2009	Travel-related infection [Resistant=74, Susceptible=24], Domestic-acquired infection [Resistant=71, Susceptible=387]			
27	Evans, 2009	18-44 [resistant=37/145, susceptible=117/411, crude OR (95%CI)=2.8 (1.1-7.7), p=0.03, Adjusted OR (95%CI)=1.5(0.5-4.0), Adjusted p=0.47], <18[resistant=7/145, susceptible=61/411]			
28	Evans, 2009	45-64 [Resistant=75/145, susceptible=152/411, crude OR (95% CI)=4.3 (1.8-11.6), p=0.004, Adjusted OR(95% CI)= 2.3 (0.9-6.2), Adjusted p=0.09], <18 [Resistant=7/145, susceptible=61/411]			
29	Evans, 2009	Resistant=0/71, Susceptible=28/359, Crude OR (95%CI)=0.0 (0.0-0.7), p=0.01			
30	Evans, 2009	Student = [Resistant=2/145, Susceptible=30/411, Crude OR (95% CI)= 0.2 (0.0-0.7), p=0.02			
31	Evans, 2009	Resistant=9/144, Susceptible=67/411, Crude OR (95% CI)=0.3 (0.2-0.7), p=0.004			
32	Evans, 2009	Resistant=5/70, Susceptible=66/387, Crude OR (95%CI)=0.4(0.1-1.0), p=0.05			
33	Evans, 2009	Male = Resistant (69/145) Susceptible (205/411) Crude OR (95%CI)=0.9 (0.6-1.4) p=0.71			
34	Evans, 2009	Employed [Resistant=84/145, Susceptible=180/411, Crude OR (95% CI)=1.8 (1.2-2.6), p=0.01]			

Factor ID	Paper REF	Result and variation	Statistical Significance (p-value):	Please provide any additional information about the factors below (Including if there is discussion about WGS)	If needed, notes about paper in general, including critical appraisal of article
35	Evans, 2009	65+ [Resistant=26/145, Suspectible=81/411, Crude OR (95% CI)=2.8 (1.1-8.1), p=0.04, adjusted OR (95% CI)=2.0(1.0-8.2), adjusted p=0.04], <18 [Resistant=7/145, Susceptible=61/411]			
36	Evans, 2009	Resistant=64/144, Susceptible=244/411, Crude OR (95%CI)=0.6(0.4-0.8), p=0.003			
37	Evans, 2009	Resistant=6/143, Susceptible=3/401, Crude OR (95% CI)=5.8(1.2-36.2), p=0.01			
38	Evans, 2009	Resistant=0/59, Susceptible=27/312, Crude OR (95% CI)=0.0 (0.0-0.7), p=0.01			
39	Evans, 2009	Resistant = 9/144, Susceptible=30/403, Crude OR (95%CI)=0.8 (0.3-1.9), p=0.77			
40	Evans, 2009	Resistant = 3/143, Susceptible = 27/408, Crude OR (95% CI)=0.3 (0.1-1.0), p=0.07, Adjusted OR=0.2 (0.0-0.9), adjusted p=0.031			
41	Evans, 2009	Resistant=35/144, Susceptible=71/405, Crude OR (95% CI)=1.5 (0.9-2.4), p=0.099			
42	Evans, 2009	Resistant = 73/128, Susceptible=293/387, Crude OR (95%CI)=0.4(0.3-0.7), p<0.001			
43	Evans, 2009	Resistant = 62/130, Susceptible=99/380, Crude OR (95%CI)=2.6 (1.7-4.0), p<0.001			
44	Evans, 2009	Resistant=19/125, Susceptible=22/379, Crude OR(95% CI)=2.9(1.4-5.9), p=0.002, Adjusted OR=3.3 (1.5-7.2), adjusted p=0.002			
45	Evans, 2009	Resistant=69/74, Susceptible=18/23, Crude OR (95% CI)=3.8 (0.8-18.4), p=0.05, Adjusted OR=5.2 (1.1-24.8), p=0.039			
46	Evans, 2009	Resistant = 11/64, Susceptible=21/363, Crude OR (95% CI)=3.4(1.4-7.8), p=0.004, Adjusted OR=3.1 (1.3-7.2), p=0.011			
47	Feodoroff, 2010	Of the 166 cases of C. jejuni infection in the study 126 were acquired abroad and 40 were acquired in Finland. Resistance to erythromycin (4 isolates) and resistance to doxycycline (59 isolates) were only detected in isolates of foreign origin. All except one of the isolates of domestic origin were susceptible for ciprofloxacin whereas 83/126 (66%) of isolates of foreign origin were resistant to ciprofloxacin			
48	Gallay, 2008	All species [Cases with resistant=10/60, Cases with susceptible=19/164; Matched controls with resistant=1/60, Matched controls with susceptible=24/164] OR (res vs sus)=1.5 (0.7-3.5)			
49	Gallay, 2008	C. jejuni [Cases with resistant=9/42, Cases with susceptible=15/142; Matched controls with resistant=0/42, Matched controls with susceptible=19/142] OR (res vs sus)=2.3(0.9-5.8)			
Factor ID	Paper REF	Result and variation	Statistical Significance (p-value):	Please provide any additional information about the factors below (Including if there is discussion about WGS)	If needed, notes about paper in general, including critical appraisal of article

50	Gaudreau, 2003	13/14 men were resistant to erythromycin, the one male who was susceptible was MSM			This study was set up to identify a possible outbreak among men in Montreal. Other factors such as HIV and travel were discussed. Genotyping was done to determine if isolates were related. As a result the MSM factor may be misleading since the study was designed with this population in mind and the comparison group is not well established (I arbitrarily decided to use those who did not disclose as MSM which may or may not accurately exclude them as MSM)
51	Gaudreau, 2003	13/14 men were susceptible to tetracycline, the 1 resistant male identified as MSM (and was the susceptible isolate to erythro)			
52	Gaudreau, 2003	3/4 men identified as N/A were resistant, 7/10 men identified as MSM were resistant			
53	Gaudreau, 2015	All 31 men were resistant to erythromycin, azithromycin, clarithromycin and clindamycin (MIC >256 mg/L)			This study was again designed to capture this population and may not be an appropriate inclusion in this study
54	Gaudreau, 2015	All 31 men were resistant to nalidixic acid (no zone around the disk)			
55	Gaudreau, 2015	All 31 men were resistant to ciprofloxacin (MIC 8-16 mg/L)			
56	Gaudreau, 2015	All 31 men were susceptible to tetracycline, ampicillin, gentimicin, and imipenem (MIC of 0.06-0.25, 0.5-1, 0.125-0.25, and 0.03 mg/L, respectively)			
57	Ghunaim, 2015	Qatari [n=72, Resistant=11.1% [5.45-20.71]]; Arabian Peninsula [n=33, Resistant=3.0% [0.39-12.95]]; Asia [n=42, Resistant=7.1% [1.78-20.39]]; Africa [n=21, Resistant=14.3% [4.01-35.43]]; Elsewhere [n=6, Resistant=0% [0-41.14]]			
58	Ghunaim, 2015	Qatari [n=72, Resistant=59.7% [47.95-70.83]]; Arabian Peninsula [n=33, Resistant=57.6% [42.87-71.27]]; Asia [n=42, Resistant=73.8% [57.28-86.05]]; Africa [n=21, Resistant=61.9% [40.33-80.26]]; Elsewhere [n=6, Resistant=66.7% [21.14-93.71]]			
59	Ghunaim, 2015	Males [n=104, Resistant=61.5% [54.43-68.16]; Females [n=70, Resistant=65.7% [54.14-75.91]			
60	Ghunaim, 2015	Males [n=104, Resistant=7.7% [4.65-12.40]]; Females [n=70, Resistant=10.0% [4.82-19.14]]			
61	Ghunaim, 2015	Age class 1 [n=34, Resistant=11.8% [4.92-24.50]]; Age class 2 [n=44, Resistant=6.8% [1.53-20.36]]; Age class 3 [n=31, Resistant= 9.7% [3.77-21.51]]; Age class 4 [n=43, Resistant=7.0% [1.65-20.37]]; Age class 5 [n=22, Resistant=9.1% [1.64-29.07]]			
Factor ID	Paper REF	Result and variation	Statistical Significance (p-value):	Please provide any additional information about the factors below (Including if there is discussion about WGS)	If needed, notes about paper in general, including critical appraisal of article
62	Ghunaim, 2015	Age class 1 [n=34, Resistant=64.7% [49.84-77.54]]; Age class 2 [n=44, Resistant=59.1% [41.97-74.63]]; Age class 3 [n=31, Resistant=67.7% [53.55-79.82]]; Age class 4 [n=43, Resistant=60.5% [43.58-84.82]]; Age class 5 [n=22, Resistant=68.2% [45.35-84.82]]			

63	Hakanen, 2003	Estimated number of trips to Finland during study months=1,145,872; Number of all isolates=77; Number of ciprofloxacin resistant isolates=55		Speculative infection rate=0.1; Speculative infection rate by cipro-resistant isolates=0.05; rate ratio of cipro-resistant isolates compared to thailand=0.11 [0.07 to 0.16] p<0.01	
64	Hakanen, 2003	Estimated number of trips from Finland during the study months=87,842; Number of all isolates=50; Number of Cipro-resistant isolates=39		Speculative infection rate=0.6; Speculative infection rate for cipro-resistant isolates=0.44	
65	Hakanen, 2003	Estimated number of trips from Finland during study period=27,591; Number of all isolates=23; Number of cipro-resistant isolates=11		Speculative infection rate=0.8; Speculative infection rate for cipro-resistant isolates=0.40; Rate ratio of cipro-resistant compared to thailand=0.90 [0.46 to 1.75]p>0.05	
66	Hakanen, 2003	Estimated number of trips from Finland during study months=25.073; Number of all isolates=12; Number of cipro-resistant isolates=8		Speculative infection rate=0.5; Speculative infection rate for cipro-resistant isolates=0.32; Rate ratio for cipro-resistant isolates compared to Thailand=0.72 [0.34 to 1.54] p>0.05	
67	Hakanen, 2003	Estimated number of trips from Finland during study period=149,647; Number of all isolates=11; Number of cipro-resistant isolates=7		Speculative infection rate=0.1; Speculative infection rate for cipro-resistant isolates=0.05; Rate ratio of cipro-resistant isolates compared to Thailand=0.11 [0.05 to 0.24] p<0.01	The five most frequent countries of origin of cipro-resistant isolates were included in this analysis To assess whether the larger proportion of isolates from Thailand during the second period explained the significant increase in fluoroquinolone resistance in the whole study group, they analysed the data excluding isolates from Thailand; the resulting increase after excluding Thailand was still significant
68	Hakanen, 2003	1995-1997=40% of 205 isolates were cipro-resistant; 1998-2000=60% of 149 isolates were cipro-resistant	p<0.01		
69	Helms, 2005	268/554 (48.4%) isolates of travel-associated infections were quinolone resistant compared to 550/2826 (19.5%) isolates of domestically acquired infections	p<0.001		The prevalence of quinolone resistance was particularly high among patients returning from Thailand (81.3%), India (71.1%), and Spain (62.5%).
70	Helms, 2005	35/554 (6.3%) isolates of the travel-associated infections compared to 163/2826 (5.8%) isolates of the domestically acquired isolates were erythromycin resistant.	p=0.61		The prevalence of erythromycin resistance was high among patients returning from India (15.8%) and Spain (10.0%).
Factor ID	Paper REF	Result and variation	Statistical Significance (p-value):	Please provide any additional information about the factors below (Including if there is discussion about WGS)	If needed, notes about paper in general, including critical appraisal of article
71	Jenkin, 1998	Only two patients had a resistant infection and both were to ciprofloxacin			This study was not set up well to extract factors related to AMR campylobacter, however it adds to the few articles about HIV patients with AMR campy. It might not have a place in this scoping review and deserves a second look, could be part of the discussion instead

72	Johnson, 2008	Our data showed foreign travel dominated any other risk factors that were examined. Furthermore, stratification of the data by regional group was important because it allowed a more detailed understanding of the risk associated with foreign travel. Cases were almost 140 times more likely than controls to have an infection acquired in Asia, but only 11 times more likely to have an infection acquired in Europe. A larger study with finer geographic groupings (e.g. by country) would probably have allowed us to capture a wide range of risk levels within macro-regions.			
73	Johnson, 2008	Female [n=95, Resistant=37.9%, Susceptible=62.1%], Male [n=114, Resistant=25.4%, Susceptible=74.6%]			
74	Johnson, 2008	<28 [n=48, Resistant=37.5%, Susceptible=62.5%], 28-37 [n=55, Resistant=21.8%, Susceptible=78.2%], 38-49 [n=53, Resistant=35.8%, Susceptible=64.2%], 50+ [n=54, Resistant=29.6%, Susceptible=70.4%]			
75	Johnson, 2008	No [n=74, Resistant=27.0%, Susceptible=73.0%], Yes [n=136, Resistant=33.1%, Susceptible=66.9%]			
76	Johnson, 2008	Summer [n=76, Resistant=17.1%, Susceptible=82.9%], Autumn [n=24, Resistant=20.8%, Susceptible=79.2%], Winter [n=28, Resistant=60.7%, Susceptible=39.3%], Spring [n=82, Resistant=36.6%, Susceptible=63.4%]			
77	Johnson, 2008	Chinook [n=41, Resistant=14.6%, Susceptible=85.4%], Calgary [n=169, Resistant=34.9%, Susceptible=65.1%]			
78	Johnson, 2008	No [n=171, Resistant=32.8%, Susceptible=67.2%], Yes [n=36, Resistant=22.2%, Susceptible=77.8%]			
79	Johnson, 2008	No [n=14, Resistant=57.1%, Susceptible=42.9%], Yes [n=196, Resistant=29.1%, Susceptible=70.9%]			Other factors such as foreign travel, broken down by Latin America, Asia and Europe, possession of non-prescribed antibiotics were also explored however the way in which the data was presented made it difficult to extract except by narrative and will be extracted in the next factor
80	Johnson, 2008	Possession was also the only risk factor identified in domestically acquired infections; further demonstrating its distinct effect in the absence of travel.			This possession factor led to questions about whether or not they took the medication, questions were also asked about non-prescribed antibiotics taken during travel as well as possessing leftover antibiotics, however follow-up questions were not asked of the participants if they took the non-prescribed antibiotics in their possession
Factor ID	Paper REF	Result and variation	Statistical Significance (p-value):	Please provide any additional information about the factors below (Including if there is discussion about WGS)	If needed, notes about paper in general, including critical appraisal of article
81	Koningstein, 2011	224/1556 [age 0-9]; 231/1150 [age 10-19]; 613/2750 [age 20-29]; 428/1958 [age 30-39]; 281/1098 [40-49]; 256/2505 [age 50-59]; 137/1436 [age 60-69]; 72/293 [age 70-79]; 26/136 [age 80+]		Sampling of age groups was not standardized to the population	Odds for a resistant strain were determined (as an interaction term in the analysis), however these results were not extracted because the control group were healthy controls, instead of susceptible. However, I believe the results may still have value despite not being extractable

82	Koningstein, 2011	25/1556 [age 0-9]; 21/1150 [age 10-19]; 57/2750 [age 20-29]; 40/1958 [age 30-39]; 32/1098 [40-49]; 32/2505 [age 50-59]; 21/1436 [age 60-69]; 8/293 [age 70-79]; 2/136 [age 80+]		Sampling of age groups was not standardized to the population	Odds for a resistant strain were determined (as an interaction term in the analysis), however these results were not extracted because the control group were healthy controls, instead of susceptible. However, I believe the results may still have value despite not being extractable
83	Kownhar, 2007	Nalidixic Acid: 1/16 HIV vs 1/5 Non-HIV			
84	Kownhar, 2007	Ciprofloxacin: 0/16 for HIV; 1/5 for Non-HIV			
85	Kownhar, 2007	Erythromycin: 0/16 for HIV; 1/5 for Non-HIV			
86	Kownhar, 2007	Trimethroprim (unclear if mixed with sulfamethoxazole so maybe this isn't relevant): 16/16 for HIV; 5/5 for Non-HIV			
87	Kownhar, 2007	Tetracyline: 0/16 for HIV; 0/5 for Non-HIV			
88	Lu, 2000	All 10 isolates stored were resistant to erythromycin, 7 were resistant to azithromycin, 8 were resistant to ceftriaxone. Of the 10 patients who were tested for susceptiblity, 7 were treated with an appropriate antimicrobial agent and 3 received an inappropriate antimicrobial agnet			
89	Nelson, 2004	Persons with cipro-resistant infection=29/70; Persons with cipro-susceptible infection=48/577, p<0.01	p<0.01		
90	Nelson, 2004	Persons with cipro-resistant infection=73/82; Persons with cipro-susceptible infection=580/654, p=1.00	1.00		
91	Nelson, 2004	Persons with cipro-resistant infection=41/81; Persons with cipro-susceptible infection=354/651, p=0.55	0.55		
92	Nelson, 2004	Persons with cipro-resistant infection=65/82; Persons with cipro-susceptible=435/655, p=0.02	p=0.02		
93	Nelson, 2004	Persons with cipro-resistant infection=51/81; Persons with cipro-susceptible infection=261/647, p<0.01	p<0.01		
94	Nelson, 2004	Persons with cipro-resistant infection=37/66; Persons with cipro-susceptible=223/547, p=0.02	p=0.02		
95	Nelson, 2004	Persons with cipro-resistant infection=4/82; Persons with cipro-susceptible infection=25/653, p=0.55	p=0.55		
Factor ID	Paper REF	Result and variation	Statistical Significance (p-value):	Please provide any additional information about the factors below (Including if there is discussion about WGS)	If needed, notes about paper in general, including critical appraisal of article
96	Patrick, 2018	Among patients with C. jejuni infection, international travel in the 7 days before infection (OR=12.5, 95% CI 10.0-15.7) was associated with resistance			
97	Patrick, 2018	Among C. coli patients, international travel in the 7 days before infection (OR=12; 95% CI 6.4-22.7) was associated with any resistance.			Among travelers with either species, the highest percentage of resistant infections was found among persons who visited Asia (18/171 (91%)) or South America (17/83 (83%)).
98	Patrick, 2018	Among patients with C. jejuni infection, age >20 (OR=1.4; 95% CI 1.1-1.8)			

99	Patrick, 2018	Among patients with C. jejuni infection, Asian race vs other (OR=2.3; 95% CI 1.4-3.9)			
100	Patrick, 2018	Resistance among C.jejuni isolates was higher in the metro (27% of 6010 isolates) compared to suburban and rural areas (15% of 6010 isolates)	p<0.0001		Mixed resistance to quinolones and macrolides
101	Patrick, 2018	Antimicrobial susceptibility information was available for 6010 C. Jejuni and 665 C. Coli isolates. Resistance to quinolones (35% vs. 24%) and macrolides (11% vs 3%) was higher among C. coli isolates than C. jejuni isolates.			
102	Patrick, 2018	Antimicrobial susceptibility information was available for 6010 C. Jejuni and 665 C. Coli isolates. Resistance to quinolones (35% vs. 24%) and macrolides (11% vs 3%) was higher among C. coli isolates than C. jejuni isolates.			
103	Perlman, 1988	The isolates from Patient 1 were intermediately susceptible to erythromycin therapy; this susceptibility remained constant throughout his illness. In contrast, Patients 2 and 3 had original isolates that were susceptible to erythromycin therapy, but during the course of their infection erythromycin-resistant isolates developed. The emergence of erythromycin-resistant isolates correlated with clinical relapse in Patient 3. For Patients 2 and 3, tetracycline therapy was begun when erythromycin-resistant isolates were detected.			
104	Ricotta, 2014	Multi/unknown destination international travel resistant =65/120; Single destination international travel resistant= 478/765; Non-international travel resistant=535/3919			For both antibiotic classes, the differences in proportion resistant between international and non---travelassociated cases were significant (ciprofloxacin OR = 9.96; 95% CI = 8.31, 11.96; P < .001; azithromycin OR = 2.76; 95% CI = 1.71, 4.38; P < .001).
105	Ricotta, 2014	Multi/unknown destination international travel resistant =5/120; Single destination international travel resistant= 28/765; Non-international travel resistant=57/3919			For both antibiotic classes, the differences in proportion resistant between international and non---travelassociated cases were significant (ciprofloxacin OR = 9.96; 95% CI = 8.31, 11.96; P < .001; azithromycin OR = 2.76; 95% CI = 1.71, 4.38; P < .001).
Factor ID	Paper REF	Result and variation	Statistical Significance (p-value):	Please provide any additional information about the factors below (Including if there is discussion about WGS)	If needed, notes about paper in general, including critical appraisal of article
106	Ricotta, 2014	(Resistant isolates/Total isolates submitted/Travelers to single destination) Africa: 28/74/295, Asia: 120/154/835, China: 18/18/101, Australia/New Zealand: 0/10/44, Central America: 53/104/490, South America: 95/115/801, Mexico: 90/145/559, Eastern Europe: 15/19/69, Western Europe: 69/139/697, North America: 2/17/87			

107	Ricotta, 2014	(Resistant isolates/Total isolates submitted/Travelers to single destination) Africa: 1/74/295, Asia: 9/154/835, China: 2/18/101, Australia/New Zealand: 0/10/44, Central America: 3/104/490, South America: 5/115/801, Mexico: 6/145/559, Eastern Europe: 1/19/69, Western Europe: 2/139/697, North America: 0/17/87			
108	Sharma, 2003	Norfloxacin [No results]; Ciprofloxacin [Overseas=43%; Locally=0%; p<0.05];			
109	Sharma, 2003	Tetracycline [Overseas=43%; Locally=10%, p<0.05]			
110	Sharma, 2003	Erythromycin [Overseas=0%, Locally=3% p>0.05]; Azithromycin [No results]; Clarithromycin [No results]; Roxithromycin [Overseas=57%, Locally=40%, p>0.05]			
111	Sharma, 2003	Nalidixic acid [Overseas=43%, Locally=1.4% ,p<0.05]			All seven isolates acquired during overseas travel were resistant to at least one class of antibiotic. There were two nalidixic acid (one with coincident ciprofloxacin resistance) and three tetracycline resistant isolates. Fifty-seven per cent (4/7) of overseas-acquired isolates were resistant to more than one antibiotic class compared to 10 per cent (14/144) of locally-acquired isolates (p=0.004, Fisher exact). Isolates acquired overseas had similar levels of ampicillin resistance to locally acquired isolates. Quinolone and tetracycline resistance were significantly more frequent in overseas isolates (Table 1). Eight per cent (12/150) of the patients took antibiotic therapy in the month prior to Campylobacter infection. The resistance rates among those exposed to antibiotics (11/12, 92%) was higher compared to unexposed subjects (109/138, 79%; Odds ratio 2.95, 95% CI 0.37-23.8, p=0.46). This was not statistically significant, possibly due to the low power to detect a difference, limited by the small sample size.
112	Skjot-Rasmussen, 2009	Travel-associated: 2006=3%, 2007=5%; Domestically-acquired: 2006=1%, 2007=0%			Values are visually estimated from the figure
113	Skjot-Rasmussen, 2009	Travel associated: 2006=36%, 2007=36%; Domestically-acquired: 2006= 15%, 2007=16%			Values are visually estimated from the figure
114	Skjot-Rasmussen, 2009	Travel associated: 2006=55%, 2007=70%; Domestically-acquired: 2006=22%, 2007=39%			Values are visually estimated from the figure
Factor ID	Paper REF	Result and variation	Statistical Significance (p-value):	Please provide any additional information about the factors below (Including if there is discussion about WGS)	If needed, notes about paper in general, including critical appraisal of article
115	Smith, 1999	Resistant=96/130; Sensitive=59/260; Univariate: Matched odds ratio (95% CI) =16.0 (7.8-38.8) p<0.001			In this matched case-comparison study, two patients with quinolone-sensitive isolates were matched for age, residence, and date of stoolspecimen collection to each patient with a quinolone-resistant isolate.
116	Smith, 1999	Resistant=47/130; Sensitive=30/260; Univariate: Matched odds ratio (95% CI) =5.6 (3.1-12.6) p<0.001; Multivariate: Matched odds ratio (95% CI) = 26.0 (8.6-78.6) p<0.001			In this matched case-comparison study, two patients with quinolone-sensitive isolates were matched for age, residence, and date of stoolspecimen collection to each patient with a quinolone-resistant isolate.

117	Smith, 1999	Resistant=14/130; Sensitive=7/260; Univariate: Matched odds ratio (95% CI) =4.5 (1.6-14.2) p<0.001; Multivariate: Matched odds ratio (95% CI) = 45.5 (9.7-214) p<0.001			In this matched case-comparison study, two patients with quinolone-sensitive isolates were matched for age, residence, and date of stoolspecimen collection to each patient with a quinolone-resistant isolate.
118	Smith, 1999	Resistant=6/130; Sensitive=44/260; Univariate: Matched odds ratio (95% CI) =0.3 (0.1-0.7) p=0.002			In this matched case-comparison study, two patients with quinolone-sensitive isolates were matched for age, residence, and date of stoolspecimen collection to each patient with a quinolone-resistant isolate.
119	Smith, 1999	Resistant=23/130; Sensitive=8/260; Univariate: Matched odds ratio (95% CI) =7.3 (2.8-21.7) p<0.001; Multivariate: Matched odds ratio (95% CI) = 40.7 (10.2-163) p<0.001			In this matched case-comparison study, two patients with quinolone-sensitive isolates were matched for age, residence, and date of stoolspecimen collection to each patient with a quinolone-resistant isolate.
120	Smith, 1999	Resistant=7/130; Sensitive=1/260; Univariate: Matched odds ratio (95% CI) =14.0 (1.8-631) p=0.001; Multivariate: Matched odds ratio (95% CI) = 48.6 (4.1-570) p=0.002			In this matched case-comparison study, two patients with quinolone-sensitive isolates were matched for age, residence, and date of stoolspecimen collection to each patient with a quinolone-resistant isolate.
121	Smith, 1999	Resistant=43/130; Sensitive=157/260; Univariate: Matched odds ratio (95% CI) =0.3 (0.2-0.6) p<0.001			In this matched case-comparison study, two patients with quinolone-sensitive isolates were matched for age, residence, and date of stoolspecimen collection to each patient with a quinolone-resistant isolate.
122	Smith, 1999	Resistant=26/130; Sensitive=7/260; Univariate: Matched odds ratio (95% CI) =7.4 (3.1-20.3) p<0.001; Multivariate: Matched odds ratio (95% CI) = 7.5 (2.6-21.3) p<0.001			In this matched case-comparison study, two patients with quinolone-sensitive isolates were matched for age, residence, and date of stoolspecimen collection to each patient with a quinolone-resistant isolate.
123	Smith, 1999	Resistant=37/130; Sensitive=48/260; Univariate: Matched odds ratio (95% CI) =2.0 (1.1-3.7) p=0.02			In this matched case-comparison study, two patients with quinolone-sensitive isolates were matched for age, residence, and date of stoolspecimen collection to each patient with a quinolone-resistant isolate.
124	Smith, 1999	Resistant=51/130; Sensitive=67/260; Univariate: Matched odds ratio (95% CI) = 2.2 (1.3-3.7) p=0.002			In this matched case-comparison study, two patients with quinolone-sensitive isolates were matched for age, residence, and date of stoolspecimen collection to each patient with a quinolone-resistant isolate.
Factor ID	Paper REF	Result and variation	Statistical Significance (p-value):	Please provide any additional information about the factors below (Including if there is discussion about WGS)	If needed, notes about paper in general, including critical appraisal of article
125	Moore, 2002	Males=6/10 Resistant to tetracycline; Females=1 Resistant, 1 Intermediate resistance, 2 Susceptible; ND=Susceptible		Some genomic data discussed	Study is a short communication, methods were sparse
126	Moore, 2002	Males=5 resistant, 2 intermediate resistance, 3 susceptible; Female=1 resistant, 1 intermediate resistance, 2 susceptible; ID=1 susceptible			
127	Uzunovic-Kamberovic, 2009	Significantly higher prevalence of resistance for both erythromycin and ciprofloxacin was observed in the isolates from the age group of 20-64 (53.8% for both antibiotics) as compared to the age group of 0-6 (23.3% for ciprofloxacin and 22.3% for erythromycin) .			Methods were unclear on how large were sample sizes of each group and which metrics were compared to reach these conclusions

128	Uzunovic-Kamberovic, 2009	Significantly higher prevalence of resistance for both erythromycin and ciprofloxacin was observed in the isolates from the age group of 20-64 (53.8% for both antibiotics) as compared to the age group of 0-6 (23.3% for ciprofloxacin and 22.3% for erythromycin) .			
129	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=92/347, Controls=82/148, OR=2.33 [1.29-4.22] p=0.0039; Logistic Reg [OR=4.95 (2.12-11.56)p<0.001]			Age and Gender also included in Logistic Regression; AGE [OR=1.00 (0.98-1.01) p=0.739] GENDER *unclear comparison, maybe male* [OR=1.01 (0.57-1.80) p=0.971]
130	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=56/347, Controls=46/148, OR=1.51 [1.00-2.29] p=0.0484			
131	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=60/347, Controls=80/148, OR=0.38 [0.23-0.62] p<0.001; Logistic Reg [OR=0.24 (0.12-0.50)p<0.001]; Interaction Term in LR with travel to Africa [OR=9.17 (1.06-79.67) p=0.044]			Age and Gender also included in Logistic Regression; AGE [OR=1.00 (0.98-1.01) p=0.739] GENDER *unclear comparison, maybe male* [OR=1.01 (0.57-1.80) p=0.971]
132	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=1/347, Controls=5/148, OR=0.14 [0.03-0.74] p=0.0069			
133	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=80/291, Controls=71/1593, OR=1.59 [1.16-22.21] p=0.004; Logistic Reg [OR=2.13 (1.44-3.13), p<0.001]			Age and Gender also included in Logistic Regression; AGE [OR=1.00 (0.99-1.01) p=0.861] GENDER *unclear comparison, maybe male* [OR=1.02 (0.76-1.38) p=0.88]
Factor ID	Paper REF	Result and variation	Statistical Significance (p-value):	Please provide any additional information about the factors below (Including if there is discussion about WGS)	If needed, notes about paper in general, including critical appraisal of article
134	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=14/291, Controls=10/1593; OR=1.44 [0.96-2.17] p=0.09			
135	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=18/291, Controls=14/1593; OR=1.37 [0.95-1.96] p=0.09			
136	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=63/291, Controls=57/1593; OR=1.29 [0.98-1.69] p=0.07			

137	Campylobacter Sentinel Surveillance Scheme, 2002	Cases= 52/291, Controls=46/1593; OR=1.25 [0.97-1.62] p=0.09			
138	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=11/291, Control=15/1593; OR=0.68 [0.44-1.06] p=0.08			
139	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=3/291, Controls=6/1593; OR=0.47 [0.20-1.10] p=0.08			
140	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=48/347, Controls=16/148, OR=4.79 [2.88-7.98] p<0.001; Logistic Reg [OR=6.87 (3.52-13.38),p<0.001]			Age and Gender also included in Logistic Regression; AGE [OR=1.00 (0.98-1.01) p=0.739] GENDER *unclear comparison, maybe male* [OR=1.01 (0.57-1.80) p=0.971]
141	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=5/347, Controls=1/148, OR=3.53 [0.80-15.64] p=0.0764; Logistic Reg [OR=11.74 (1.28-108.02),p=0.03]			Age and Gender also included in Logistic Regression; AGE [OR=1.00 (0.98-1.01) p=0.739] GENDER *unclear comparison, maybe male* [OR=1.01 (0.57-1.80) p=0.971]
Factor ID	Paper REF	Result and variation	Statistical Significance (p-value):	Please provide any additional information about the factors below (Including if there is discussion about WGS)	If needed, notes about paper in general, including critical appraisal of article
142	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=8/347, Controls=3/148, OR=3.04 [1.04-8.89] p=0.0329; Logistic Reg[OR=22.40 (4.36,114.99), p<0.001]			Age and Gender also included in Logistic Regression; AGE [OR=1.00 (0.98-1.01) p=0.739] GENDER *unclear comparison, maybe male* [OR=1.01 (0.57-1.80) p=0.971]
143	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=3/347, Controls=6/148, OR=0.41 [0.16-1.06] p=0.058			
144	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=4/347, Control=11/148, OR=0.35 [0.16-0.74] p=0.0039			
145	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=3/347, Control=13/148, OR=0.24 [0.11-0.52] p=0.0001, Logistic Reg [OR=0.11 (0.02-0.70) p=0.019]; Interaction Term in LR with consumption of mains water [OR=9.17 (1.06-79.67) p=0.044]		Morocco (55%); Tunisia (19%); South Africa (10%); Kenya (6%); Mauritius (6%); Tanzania (3%).	Age and Gender also included in Logistic Regression; AGE [OR=1.00 (0.98-1.01) p=0.739] GENDER *unclear comparison, maybe male* [OR=1.01 (0.57-1.80) p=0.971]

146	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=22/291, Controls=38/1593; OR=0.44 [0.32-0.60] p<0.001; Logistic Reg [OR=0.46 (0.33-0.65), p<0.001]			Age and Gender also included in Logistic Regression; AGE [OR=1.00 (0.99-1.01) p=0.861] GENDER *unclear comparison, maybe male* [OR=1.02 (0.76-1.38) p=0.88]
147	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=2/291, Control=5/1593; OR=0.47[0.22-1.03] p=0.05			
148	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=6/291, Controls=3/1593; OR=1.71 [0.96-3.04] p=0.06			
149	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=22/291, Controls=17/1593; OR=1.32 [0.96-1.80] p=0.08			
Factor ID	Paper REF	Result and variation	Statistical Significance (p-value):	Please provide any additional information about the factors below (Including if there is discussion about WGS)	If needed, notes about paper in general, including critical appraisal of article
150	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=32/291, Controls=23/1593; OR=1.60 [1.21-2.12] p=0.0008			
151	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=25/291, Controls=17/1593; OR=1.67 [1.24-2.26] p=0.0007		Logistic regression analysis is available for the indigenous acquired c. jejuni infection in table 4	
152	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=48/347, Controls=64/148, OR=0.52 [0.34-0.77] p=0.0011			
153	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=20/347, Controls=27/148, OR=0.65 [0.39-1.07] p=0.0883			
154	Campylobacter Sentinel Surveillance Scheme, 2002	Cases= 1/347, Controls=6/148, OR=0.21 [0.06-0.75] p=0.0078; Logistic Reg [OR=0.11 (0.02-0.58) p=0.009]			Age and Gender also included in Logistic Regression; AGE [OR=1.00 (0.98-1.01) p=0.739] GENDER *unclear comparison, maybe male* [OR=1.01 (0.57-1.80) p=0.971]

155	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=2/347, Controls=5/148, OR=0.38 [0.12-1.20] p=0.0864			
156	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=<1/347, Controls=4/148, OR=0.10 [0.01-0.90] p=0.0106			
157	Campylobacter Sentinel Surveillance Scheme, 2002	Cases= 1/291, Controls=3/1593; OR=0.21[0.03-1.57] p=0.09			
Factor ID	Paper REF	Result and variation	Statistical Significance (p-value):	Please provide any additional information about the factors below (Including if there is discussion about WGS)	If needed, notes about paper in general, including critical appraisal of article
158	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=90/347, Controls=80/148, OR=2.28 [1.30-4.00] p=0.0031; Logistic Reg [OR=3.70 (1.69-8.10) p=0.001]			Age and Gender also included in Logistic Regression; AGE [OR=1.00 (0.98-1.01) p=0.739] GENDER *unclear comparison, maybe male* [OR=1.01 (0.57-1.80) p=0.971]
159	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=11/347, Controls=18/148, OR=0.56 [0.31-1.02] p=0.0539			
160	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=59/347, Controls=49/148, OR=1.47 [0.99-2.17] p=0.0531			
161	Campylobacter Sentinel Surveillance Scheme, 2002	Cases=4/291, Controls=8/1593; OR=0.45 [0.22-0.94] p=0.03			
162	WonHee, 2016	Univariate: OR=0.082 [0.0095-0.71] p=0.0095; Multivariate: not included			Consumption of home prepared chicken was a significant protective factor by univariate analysis; however, it was not used for multivariate analysis because of the small sample size left when the characteristic was included in the base model
163	WonHee, 2016	Univariate: OR=35.7 [5.78-220.38] p<0.0001; Multivariate: OR=33.4 [3.9-285.2] p=0.0013		Genomic data may be available	Table 3 was specifically for fluoroquinolone resistant campylobacter, Table 2 indicates that only 18/94 isolates were resistant to fluoroquinolone/ciprofloxacin instead of the 64/94 isolates that were resistant to at least one antimicrobial tested
164	WonHee, 2016	Univariate: OR=0.92 [0.32-2.68] p=0.88; Multivariate: Not included			
165	WonHee, 2016	Univariate: OR=3.27 [0.92-11.58] p=0.056; Multivariate: OR=8.1 [0.9-72.7] p=0.0614			

166	WonHee, 2016	Univariate: Not included; Multivariate: OR=1.05 [0.99-1.1] p=0.0536			
167	WonHee, 2016	Univariate: OR=0.37 [0.10-1.33] p=0.19; Multivariate: OR=0.26 [0.041-1.659] p=0.1542			
168	van Hees, 2007	Endemic=2179/6520 resistant; Travel-related=351/645 resistant			
169	van Hees, 2007	Endemic=960/4897 resistant; Travel-related=132/487 resistant			While unclear about what the comparison group was used and to which antimicrobials were used, factors related to age, gender, geographical location, temporal infection and seasonal trends were all documented in addition to endemic vs travel. However due to their unclear nature, these factors were not extracted individually
170	van Hees, 2007	Endemic=94/5739 resistant; Travel-related=12/568 resistant			

APPENDIX 2.3

Data Extraction Form

[In the following pages]

Submit Form and go to [ ] or Skip to Next

1. What is the year of publication?

...

2. What year(s) were the data collected? (format: mm/dd/yy-mm/dd/yy)

...

3. What is the study design?

Select an Answer

Permanently add an answer to this question

4. How was participant information collected?

Select an Answer

Permanently add an answer to this question

5. What is/are the study objectives?

6. What is the method used for antimicrobial susceptibility testing

Broth MICROdilution	Broth MACROdilution	Disk Diffusion	Gradient Diffusion	Agar Dilution	PCR
WGS	Not Reported	Other, specify		Agar Diffusion	E-test

Permanently add an answer to this question

7. What MIC interpretive criteria was used?

Select an Answer

Permanently add an answer to this question

8. What country was the study population included from?

Select an Answer

Permanently add an answer to this question
Clear Response

9. What was the population(s) sampled?

10. What was the total sample size?

...

11. What is the comparison group?

12. What is the sample size of the comparison group?

...

13. How was the population/participants identified?
[IE: Cases? Hospitalized or seeking medical attention? From a notifiable database? File Review?]

14. What are the age details for the total sample? (eg. average age, range, etc.)

...

15. What were the proportion of females and/or males included in the study? (%, calculated during extraction if necessary)

Female		Male		Not specified	

16. What were the participant selection methods?

17. How many factors related to antimicrobial resistant *Campylobacter*were investigated/identified?

...

18. Definition of the factor:

19. What is the sample size of the exposed group?

...

20. Reported format:

Select an Answer

Permanently add an answer to this question

21. Campylobacter species

Select an Answer

22. What types of infection are reported in the study?

Select an Answer

23. Specify the type of resistant infection (a new form will be needed for each type of resistant infection):

Select an Answer

24. Type of analysis:

- ☐ Univariate Linear Regression
- ☐ Multiple Linear Regression
- ☐ Multivariate Regression
- ☐ Logistic Regression
- ☐ Factor Analysis
- ☐ Survival Analysis
- ☐ Other, specify

25. Type of Result:

Select an Answer

26. Result and variation

...

27. Statistical Significance (p-value):

...

28. Please provide any additional information about the factors below (Including if there is discussion about WGS)

29. If needed, notes about paper in general, including critical appraisal of article

APPENDIX 3.1

Overall iAM.AMR Search Strategy

[In the following pages]

AMR in livestock for meat consumption – Kaitlin Young

Search completed by Kate Merucci on April 15, 2019

RefWorks: colleen.murphy2 // colleen

If you're planning to publish your article or report, please acknowledge the Health Library in your publication. Acknowledging the Health Library demonstrates the value of our staff and collections that support the high quality work produced by Health Canada and the Public Health Agency. The Health Library can also assist in preparing search methodologies. Contact us for more information.

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SEARCH STRATEGY

Articles were exported on April 11, 2019

MEDLINE

Database(s): **Ovid MEDLINE(R) ALL** 1946 to April 10, 2019
Search Strategy:

#	Searches	Results
1	exp *Drug Resistance, Microbial/ or exp *Drug Resistance, Multiple/	70939
2	((resistan* adj4 (antimicrobial* or microbial* or antibiotic* or anti biotic* or antibacterial* or bacteria* or multidrug* or multi drug* or extensively drug or multiple drug* or multiclass* or multi class* or multiple class*)) or amr).ti,kf,kw. or ((resistan* adj4 (antimicrobial* or microbial* or antibiotic* or anti biotic* or antibacterial* or bacteria* or multidrug* or multi drug* or extensively drug or multiple drug* or multiclass* or multi class* or multiple class*)) or amr).ab. /freq=2	80816
3	exp *beta-Lactams/ or *tetracycline/ or exp *quinolones/ or exp *macrolides/ or exp *nalidixic acid/ or exp *ciprofloxacin/ or *enrofloxacin/	170367
4	("B-lactam*" or "beta-lactam*" or penicillin* or carbapenem* or cephalosporin* or moxalactam* or latamoxef* or tetracycline or quinolone* or "4-Quinolone*" or fluoroquinolone* or macrolide* or tylosin* or ciprofloxacin* or enrofloxacin*).ti,ab,kw,kf.	176942
5	or/1-4 [AMR]	354638
6	*cattle/ or exp *swine/ or *chickens/ or *turkeys/ or (cattle or cow? or bull or bulls or steer? or calf or calves or bos taurus or beef or veal or pig? or piglet? or swine? or hog? or sow? or pork or sus scrofa domesticus or chick? or chicken? or rooster? or hen? or broiler? or gallus gallus domesticus or turkeys or meleagris gallopavo or turkey or gobbler? or poultr*).ti,kf,kw. or (cattle or cow? or bull or bulls or steer? or calf or calves or bos taurus or beef or veal or pig? or piglet? or swine? or hog? or sow? or pork or sus scrofa domesticus or chick? or chicken? or rooster? or hen? or broiler? or gallus gallus domesticus or turkeys or meleagris gallopavo or turkey or gobbler? or poultr*).ab. /freq=2	494578
7	exp *Escherichia coli/ or (Escherichia coli or "e coli" or ecoli).ti,kf,kw. or (Escherichia coli or "e coli" or ecoli).ab. /freq=2	199672

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8	exp *salmonella/ or salmonella.ti,kw,kf. or salmonella.ab. /freq=2	56026
9	exp *Campylobacter/ or campylobacter.ti,kw,kf. or campylobacter.ab. /freq=2	12470
10	*Enterococcus faecium/ or (enterococcus faecium or "e faecium").ti,kw,kf. or (enterococcus faecium or "e faecium").ab. /freq=2	3887
11	*Enterococcus faecalis/ or (Enterococcus faecalis or "e faecalis").ti,kw,kf. or (Enterococcus faecalis or "e faecalis").ab. /freq=2	8213
12	or/7-11	270276
13	and/5-6,12	3834

EMBASE

Database(s): **Embase** 1974 to 2019 April 09
Search Strategy:

#	Searches	Results
1	exp *antibiotic resistance/ or *multidrug resistance/ or *cross resistance/	68099
2	((resistan* adj4 (antimicrobial* or microbial* or antibiotic* or anti biotic* or antibacterial* or bacteria* or multidrug* or multi drug* or extensively drug or multiple drug* or multiclass* or multi class* or multiple class*)) or amr).ti,kw. or ((resistan* adj4 (antimicrobial* or microbial* or antibiotic* or anti biotic* or antibacterial* or bacteria* or multidrug* or multi drug* or extensively drug or multiple drug* or multiclass* or multi class* or multiple class*)) or amr).ab. /freq=2	102496
3	*beta lactam/ or *beta lactam antibiotic/ or *beta-lactam resistance/ or exp *penicillin derivative/ or exp *penicillin resistance/ or *carbapenem/ or *carbapenem derivative/ or *cephalosporin derivative/ or *cephalosporin resistance/ or *quinolone derivative/ or exp *macrolide/ or *ciprofloxacin/	175250
4	("B-lactam*" or "beta-lactam*" or penicillin* or carbapenem* or cephalosporin* or moxalactam* or latamoxef* or tetracycline* or quinolone* or "4-Quinolone*" or fluoroquinolone* or macrolide* or tylosin* or ciprofloxacin* or enrofloxacin*).ti,ab,kw.	203229
5	or/1-4	397288
6	(exp *bovine/ or exp *pig/ or exp *chicken/ or exp *"turkey (bird)"/) and *meat/	948
7	*chicken meat/ or *turkey meat/ or *pork/ or *veal/ or *beef/ or (broiler? or beef or veal or pork or bull or bulls or steer? or pig? or piglet? or swine? or hog? or sow? or turkeys or meleagris gallopavo or turkey or gobbler? or rooster? or sus scrofa domesticus or bos taurus or gallus gallus domesticus or cattle or cow? or calf or calves or chick? or chicken? or hen? or poultr*).ti,kw. or (broiler? or beef or veal or pork or bull or bulls or steer? or pig? or piglet? or swine? or hog? or sow? or turkeys or meleagris gallopavo	457406

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	or turkey or gobbler? or rooster? or sus scrofa domesticus or bos taurus or gallus gallus domesticus or cattle or cow? or calf or calves or chick? or chicken? or hen? or poultr*).ab. /freq=2	
8	6 or 7	457453
9	exp *Escherichia coli/ or (Escherichia coli or "e coli" or ecoli).ti,kw. or (Escherichia coli or "e coli" or ecoli).ab. /freq=2	200664
10	exp *salmonella/ or salmonella.ti,kw. or salmonella.ab. /freq=2	49288
11	exp *Campylobacter/ or campylobacter.ti,kw. or campylobacter.ab. /freq=2	13929
12	*Enterococcus faecium/ or (enterococcus faecium or "e faecium").ti,kw. or (enterococcus faecium or "e faecium").ab. /freq=2	4305
13	*Enterococcus faecalis/ or (Enterococcus faecalis or "e faecalis").ti,kw. or (Enterococcus faecalis or "e faecalis").ab. /freq=2	9122
14	or/9-13	266000
15	and/5,8,14	3985

AGRICOLA

Database(s): **AGRICOLA** 1970 to March 2019
Search Strategy:

#	Searches	Results
1	antibiotic resistance/ or multiple drug resistance/	7019
2	((resistan* adj4 (antimicrobial* or microbial* or antibiotic* or anti biotic* or antibacterial* or bacteria* or multidrug* or multi drug* or extensively drug or multiple drug* or multiclass* or multi class* or multiple class*)) or amr).tw,hw.	23658
3	beta-lactam antibiotics/ or beta-lactamase/ or exp penicillins/ or exp cephalosporins/ or exp quinolones/ or exp tetracyclines/ or exp macrolides/	10362
4	("b-lactam*" or "beta-lactam*" or penicillin* or carbapenem* or cephalosporin* or moxalactam* or latamoxef* or tetracycline* or quinolone* or "4-Quinolone*" or fluoroquinolone* or macrolide* or tylosin* or ciprofloxacin* or enrofloxacin*).tw,hw.	17762
5	or/1-4	39252
6	(exp cattle/ or exp swine/ or exp chickens/ or exp turkeys/) and (meat/ or exp meat products/ or meat production/)	7213
7	exp chicken meat/ or exp poultry skin/ or exp turkey meat/ or exp pork/ or exp beef/ or (cattle or cow? or bull or bulls or steer? or calf or calves or bos taurus or beef or veal or pig? or piglet? or swine? or hog? or sow? or pork or sus scrofa domesticus or chick? or chicken? or rooster? or hen? or broiler? or	507940

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	gallus gallus domesticus or turkeys or meleagris gallopavo or turkey or gobbler? or poultr*).tw,hw.	
8	6 or 7	507955
9	exp escherichia coli/ or (escherichia coli or "e coli" or ecoli).tw,hw.	64875
10	exp salmonella/ or salmonella.tw,hw.	22156
11	exp campylobacter/ or campylobacter.tw,hw.	4894
12	enterococcus faecium/ or (enterococcus faecium or "e faecium").tw,hw.	1816
13	enterococcus faecalis/ or (enterococcus faecalis or "e faecalis").tw,hw.	2410
14	or/9-13	87187
15	and/5,8,14	2525

CAB ABSTRACTS

Database(s): **CAB Abstracts** 1973 to 2019 Week 13
Search Strategy:

#	Searches	Results
1	exp drug resistance/	55766
2	((resistan* adj4 (antimicrobial* or microbial* or antibiotic* or anti biotic* or antibacterial* or bacteria* or multidrug* or multi drug* or extensively drug or multiple drug* or multiclass* or multi class* or multiple class*)) or amr).ti,hw. or ((resistan* adj4 (antimicrobial* or microbial* or antibiotic* or anti biotic* or antibacterial* or bacteria* or multidrug* or multi drug* or extensively drug or multiple drug* or multiclass* or multi class* or multiple class*)) or amr).ab. /freq=2	29968
3	exp beta-lactam antibiotics/ or latamoxef/ or exp tetracyclines/ or quinolones/ or macrolide antibiotics/ or exp fluoroquinolone antibiotics/	65859
4	("b-lactam*" or "beta-lactam*" or penicillin* or carbapenem* or cephalosporin* or moxalactam* or latamoxef* or tetracycline* or quinolone* or "4-Quinolone*" or fluoroquinolone* or macrolide* or tylosin* or ciprofloxacin* or enrofloxacin*).ti,hw. or ("b-lactam*" or "beta-lactam*" or penicillin* or carbapenem* or cephalosporin* or moxalactam* or latamoxef* or tetracycline* or quinolone* or "4-Quinolone*" or fluoroquinolone* or macrolide* or tylosin* or ciprofloxacin* or enrofloxacin*).ab. /freq=2	68372
5	or/1-4	110329
6	(meat/ or exp meat cuts/ or exp meat products/) and (exp cattle/ or exp pigs/	18945

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	or exp turkeys/ or exp fowls/)	
7	exp beef cattle/ or exp pigmeat/ or chicken meat/ or turkey meat/ or (broiler? or beef or pork or veal or bos taurus or sus scrofa domesticus or gallus gallus domesticus or meleagris gallopavo).ti,hw. or (broiler? or beef or pork or veal or bos taurus or sus scrofa domesticus or gallus gallus domesticus or meleagris gallopavo).ab. /freq=2	146697
8	((cattle or cow? or bull or bulls or steer? or calf or calves or pig? or piglet? or swine? or hog? or sow? or chick? or chicken? or rooster? or hen? or turkeys or turkey or gobbler? or poultr*) adj5 (meat? or food or foods or consum* or eat or eaten or slaughter* or butcher*)).ti,hw. or ((cattle or cow? or bull or bulls or steer? or calf or calves or pig? or piglet? or swine? or hog? or sow? or chick? or chicken? or rooster? or hen? or turkeys or turkey or gobbler? or poultr*) adj5 (meat? or food or foods or consum* or eat or eaten or slaughter* or butcher*)).ab. /freq=2	50286
9	or/6-8	177656
10	exp escherichia coli/ or (escherichia coli or "e coli" or ecoli).ti,hw. or (escherichia coli or "e coli" or ecoli).ab. /freq=2	95967
11	exp salmonella/ or salmonella.ti,hw. or salmonella.ab. /freq=2	52993
12	exp campylobacter/ or campylobacter.ti,hw. or campylobacter.ab. /freq=2	11468
13	enterococcus faecium/ or (enterococcus faecium or "e faecium").ti,hw. or (enterococcus faecium or "e faecium").ab. /freq=2	4085
14	enterococcus faecalis/ or (enterococcus faecalis or "e faecalis").ti,hw. or (enterococcus faecalis or "e faecalis").ab. /freq=2	6655
15	or/10-14	145742
16	and/5,9,15	2893

FOOD SCIENCE AND TECHNOLOGY ABSTRACTS

Database(s): **Food Science and Technology Abstracts** 1969 to 2019 April Week 1
Search Strategy:

#	Searches	Results
1	ANTIBIOTICS RESISTANCE/	6095
2	((resistan* adj4 (antimicrobial* or microbial* or antibiotic* or anti biotic* or antibacterial* or bacteria* or multidrug* or multi drug* or extensively drug or multiple drug* or multiclass* or multi class* or multiple class*)) or amr).tw,hw.	10433
3	beta-LACTAM ANTIBIOTICs/ or beta-LACTAMASES/ or exp TETRACYCLINES/ or exp QUINOLONES/ or exp MACROLIDE ANTIBIOTICS/	2519
4	("b-lactam*" or "beta-lactam*" or penicillin* or carbapenem* or cephalosporin* or moxalactam* or latamoxef* or tetracycline* or quinolone* or "4-Quinolone*" or fluoroquinolone* or macrolide* or tylosin* or ciprofloxacin* or enrofloxacin*).tw,hw.	8095
5	or/1-4	14975
6	(exp meat/ or meat products/) and (exp cattle/ or exp swine/ or chickens/ or turkeys/)	20903
7	exp beef/ or exp veal/ or exp pork/ or exp chicken meat/ or exp turkey meat/ or (broiler? or beef or pork or veal or bos taurus or sus scrofa domesticus or gallus gallus domesticus or meleagris gallopavo).tw,hw.	73072
8	(cattle or cow? or bull or bulls or steer? or calf or calves or pig? or piglet? or swine? or hog? or sow? or chick? or chicken? or rooster? or hen? or turkeys or turkey or gobbler? or poultr*).ti,hw. or (cattle or cow? or bull or bulls or steer? or calf or calves or pig? or piglet? or swine? or hog? or sow? or chick? or chicken? or rooster? or hen? or turkeys or turkey or gobbler? or poultr*).ab. /freq=2	90981
9	or/6-8	121712
10	ESCHERICHIA COLI/ or (escherichia coli or "e coli" or ecoli).tw,hw.	36688
11	exp SALMONELLA/ or salmonella.tw,hw.	25417
12	exp campylobacter/ or campylobacter.tw,hw.	5666
13	ENTEROCOCCUS FAECIUM/ or (enterococcus faecium or "e	1637

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	faecium").tw,hw.	
14	ENTEROCOCCUS FAECALIS/ or (enterococcus faecalis or "e faecalis").tw,hw.	1740
15	or/10-14	59654
16	and/5,9,15	2366

SEARCH REQUEST

From: Young, Kaitlin (PHAC/ASPC)
Sent: 2019-02-26 14:03
To: Library / Bibliothèque (HC/SC)
Cc: Murphy2, Colleen (PHAC/ASPC)
Subject: Literature Search Help

Good Afternoon,

I am a Master of Public Health student working with the Canadian Integrated Program for Antimicrobial Resistance of PHAC. As part of my practicum placement I am helping with updating a literature search that identifies studies investigating factors potentially linked with antimicrobial resistance in Campylobacter species, Escherichia coli, and Salmonella enterica along the farm-to-fork pathway (farm, abattoir (slaughter houses) and retail meats) for the major Canadian livestock species (beef cattle, broiler chicken, pig, and turkey).

Below is the search string we were thinking of using for this update:
((((Antimicrobial[Title/Abstract] OR Antibiotic[Title/Abstract]) AND (Resistance[Title/Abstract] OR Susceptibility[Title/Abstract])) AND (B-lactam$[All Fields] OR ("cephalosporins"[MeSH Terms] OR "cephalosporins"[All Fields] OR "cephalosporin"[All Fields]) OR ("tetracycline"[MeSH Terms] OR "tetracycline"[All Fields]) OR ("quinolones"[MeSH Terms] OR "quinolones"[All Fields] OR "quinolone"[All Fields]) OR ("fluoroquinolones"[MeSH Terms] OR "fluoroquinolones"[All Fields] OR "fluoroquinolone"[All Fields]) OR ("macrolides"[MeSH Terms] OR "macrolides"[All Fields] OR "macrolide"[All Fields]) OR ("nalidixic acid"[MeSH Terms] OR ("nalidixic"[All Fields] AND "acid"[All Fields]) OR "nalidixic acid"[All Fields]) OR ("ciprofloxacin"[MeSH Terms] OR "ciprofloxacin"[All Fields] OR (“enrofloxacin” [MeSH Terms] OR “enrofloxacin” [All Fields])))) AND (cow$[Title/Abstract] OR cattle[Title/Abstract] OR beef[Title/Abstract] OR dairy[Title/Abstract] OR pig$[Title/Abstract] OR sow$[Title/Abstract] OR piglet$[Title/Abstract] OR pork[Title/Abstract] OR chicken$[Title/Abstract] OR broiler$[Title/Abstract] OR chick$[Title/Abstract] OR turkey$ss[Title/Abstract]) AND (E. coli[Title/Abstract] OR Escherichia coli [Title/Abstract] OR Salmonella[Title/Abstract] OR Campylobacter[Title/Abstract])

We are wondering if we could talk to a resource at the Health Library about helping us with this search? We would also be open to suggestions for ways to refine our search strings to maximize specificity.

Thanks,
Kaitlin Young, BSc, MPH

From: Merucci, Katherine (HC/SC)
Sent: 2019-02-26 2:39 PM
To: Young, Kaitlin (PHAC/ASPC)
Cc: Murphy2, Colleen (PHAC/ASPC); Glandon, Lisa (HC/SC)
Subject: RE: Literature Search Help

Hi Kaitlin,

Do you have a copy of the original search? Generally for an update, you would use the original search as is and change the date limits.

For this search however, we do recommend some tweaks to maximize relevancy. Was the original search completed in other databases?

We can also discuss this search over the phone if that's more convenient for you.

Thanks,

Kate Merucci, MLIS

From: Murphy2, Colleen (PHAC/ASPC)
Sent: 2019-02-26 16:08
To: Merucci, Katherine (HC/SC)
Subject: RE: Literature Search Help

Hi Kate
I am happy to chat with you regarding the search and how it was done previously and what we are looking for now.
Are you available Thursday? I have availability between 11 am and 1:30 pm.
Thanks
Colleen

Colleen Murphy DVM MSc PhD
Veterinary Epidemiologist
Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS)
Centre for Food-borne, Environmental and Zoonotic Infectious Diseases
Public Health Agency of Canada

- Cattle, pigs, chickens, turkeys (no dairy or eggs)

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- AMR against ecoli, salmonella, campylobacter (all species)
- Last 5 years
- (Antimicrobial OR specific antibiotics) AND resistance
- Farm to table

From: Murphy2, Colleen (PHAC/ASPC)
Sent: 2019-03-19 16:32
To: Merucci, Katherine (HC/SC)
Cc: Chapman, Brennan (PHAC/ASPC)
Subject: RE: AMR in livestock prelim search results

Hi Kathrine
I have not forgot about this request.
We had a meeting today and discussed the search and our needs.
I have also included Brennan Chapman on this conversation. He is a PhD student working with us and he will take a big role in the search, screening, data extraction. I just wanted to use this as an opportunity to introduce you.
Can the we add in terms to return results for veal?
And can we add in terms for Enterococcus for all the animal populations.
We are largely interested in Enterococcus faecium and Enterococcus faecalis.
However, I am not sure if it is better to specify the species (faecium, faecalis) in the search or leave it just as the genus (Enterococcus). And this could be impacted by animal population as well (for example- maybe better to speciate with chickens, but maybe not with cattle)
Are you able to help us with this?
Thanks so much
Colleen

From: Merucci, Katherine (HC/SC)
Sent: 2019-03-20 8:57 AM
To: Murphy2, Colleen (PHAC/ASPC)
Cc: Chapman, Brennan (PHAC/ASPC)
Subject: RE: AMR in livestock prelim search results

Hi Colleen,

Veal was included in the original search, but if you have additional meat terms you would like to use just let me know!

We can go broad with enterococcus, but I would still list all the species in the keywords as well. For example, it would like something like (enterococcus or “e faecalis” or “e faecium” or “e alcedinis” or etc.) This would make sure we’re capturing everything even if authors don’t spell out enterococcus and just use the shortened “e.”

However, if you're primarily interested in e. faceium and e. faecalis, I would recommend just looking at those two.

I can separate the search out by animal, but I will need some direction as to how you want to separate them. This may not be necessary unless you're getting a lot of irrelevant results.

Thanks,

Kate Merucci

From: Murphy2, Colleen (PHAC/ASPC)
Sent: 2019-03-20 09:07
To: Merucci, Katherine (HC/SC)
Cc: Chapman, Brennan (PHAC/ASPC)
Subject: RE: AMR in livestock prelim search results

Thanks so much.
Let's limit the search to faecium and faecalis for enterococcus. There are a number of enterococcus species, but we are most interested in the species with zoonotic potential (from the animal populations of interest), rather than animal specific potential pathogens.
Let's not separate by animal population yet-I think we should look at the results first.
Does this sound reasonable?
Just curious-do you have an input on using abstactr for screening. Unfortunately, we do not have access to DistillerSR.
Brennan found this and it seems like it maybe better than our cobbled-together excel sheet that was used in 2014 at the beginning of this project.
Thanks
Colleen

APPENDIX 3.2

Data Extraction Forms for the iAM.AMR

[In the following pages]

Add or Edit a Reference

Distribution and characterization of ampicillin- and tetracycline-resistant Escherichia coli from feedlot cattle fed subtherapeutic antimicrobials

Open Factor List

BMC Microbiology

Reference ID: 00043

Found in 2016 ☑ Number of Factors 24

Found in 2019 ☐ Study Location CAN

Found via Snowball ☐ Reference Status:

Found via Submit ☐

Basic Info | Study Info | Location | Auditing | Notes and Issues

Status:

Reference Status:

Description:

Bibliographic Information:

name_bibtex

Author Name(s)	Mirzaagha, Louie, Sharma, Yanke, Topp, McAllister
Pub Year	2011
Publisher	BMC Microbiology
Title	Distribution and characterization of ampicillin- and tetracycline-resistant Escherichia coli from feedlot cattle fed subtherapeutic antimicrobials
Abstract	Feedlot cattle in North America are routinely fed subtherapeutic levels of antimicrobials to prevent disease and improve the efficiency of growth. This practice has been shown to promote antimicrobial resistance (AMR) in subpopulations of intestinal microflora including Escherichia coli. To date, studies of AMR in feedlot production settings have rarely employed selective isolation, therefore yielding too few AMR isolates to enable characterization of the emergence and nature of AMR in E. coli as an indicator bacterium. E. coli isolates (n = 531) were recovered from 140 cattle that were housed (10 animals/pen) in 14 pens and received no dietary antimicrobials (control--5 pens, CON), or were intermittently administered subtherapeutic levels of chlortetracycline (5 pens-T), chlortetracycline + sulfamethazine (4 pens-TS), or virginiamycin (5 pens-V) for two separate periods over a 9-month feeding period. Phenotype and genotype of the isolates were determined by susceptibility testing and pulsed field gel electrophoresis and distribution of characterized isolates among housed cattle reported. It was hypothesized that the feeding of subtherapeutic antibiotics would increase the isolation of distinct genotypes of AMR E. coli from cattle.

Basic Info | Study Info | Location | Auditing | Notes and Issues

Study Identifiers:

DOI: 10.1186/1471-2180-11-78

PMID:

Study Design:

Design: Experimental

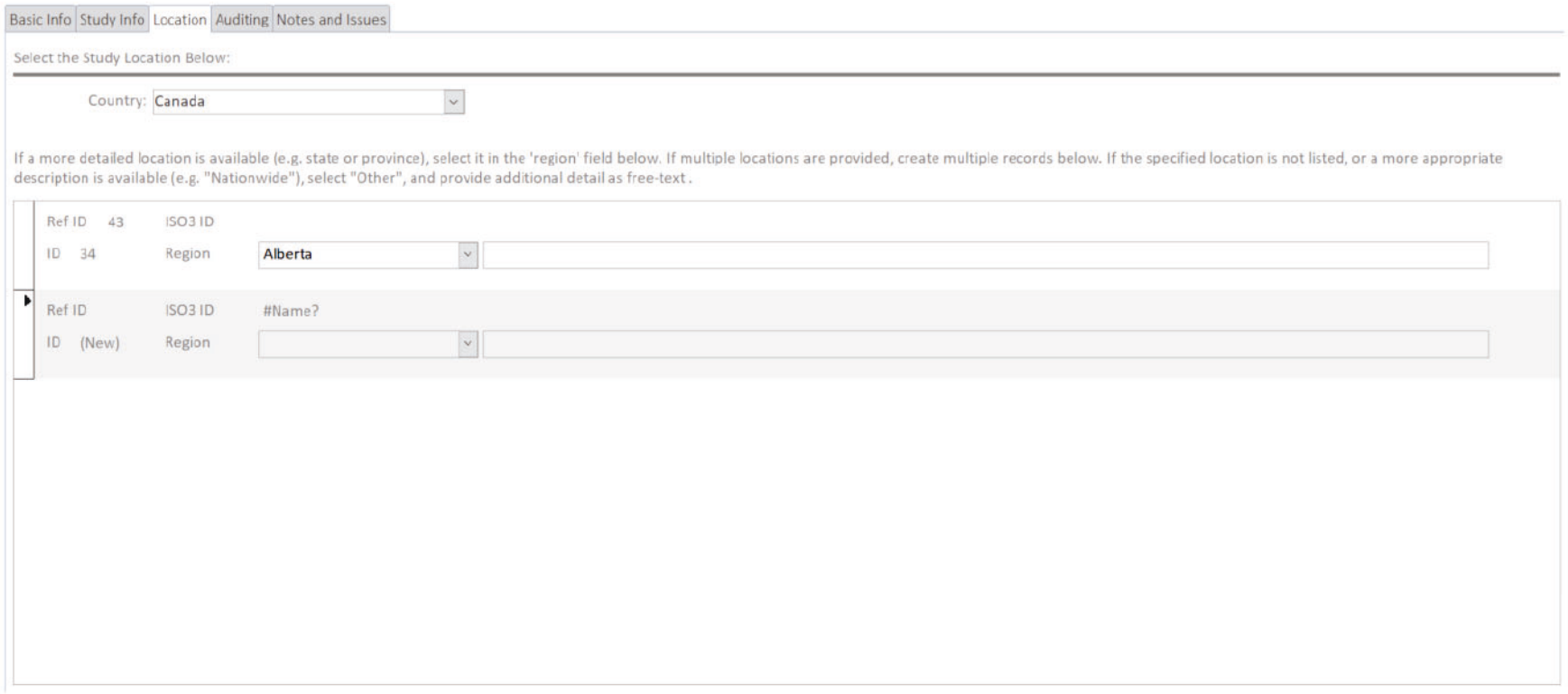
Design Detail: The study included six experimental treatments (control plus five different dietary antibiotics), each fed to five pens of 10 cattle with the exception of the Aureo S-700G treatment which only had four replicate pens. The treatments included the control group (CON; no antibiotics added to supplement) and three of the five antibiotic treatment groups: 1) chlortetracycline (T), provided as Aureomycin 100-G fed at 11 ppm; 2) chlortetracycline + sulfamethazine (TS), provided as Aureo S-700G fed at 44 ppm; 3) virginiamycin (V), provided as V-Max fed at 31 ppm. The antimicrobial agents were selected based on the commonality of their use in the Canadian feedlot industry and were fed at the concentrations recommended by the manufacturers.

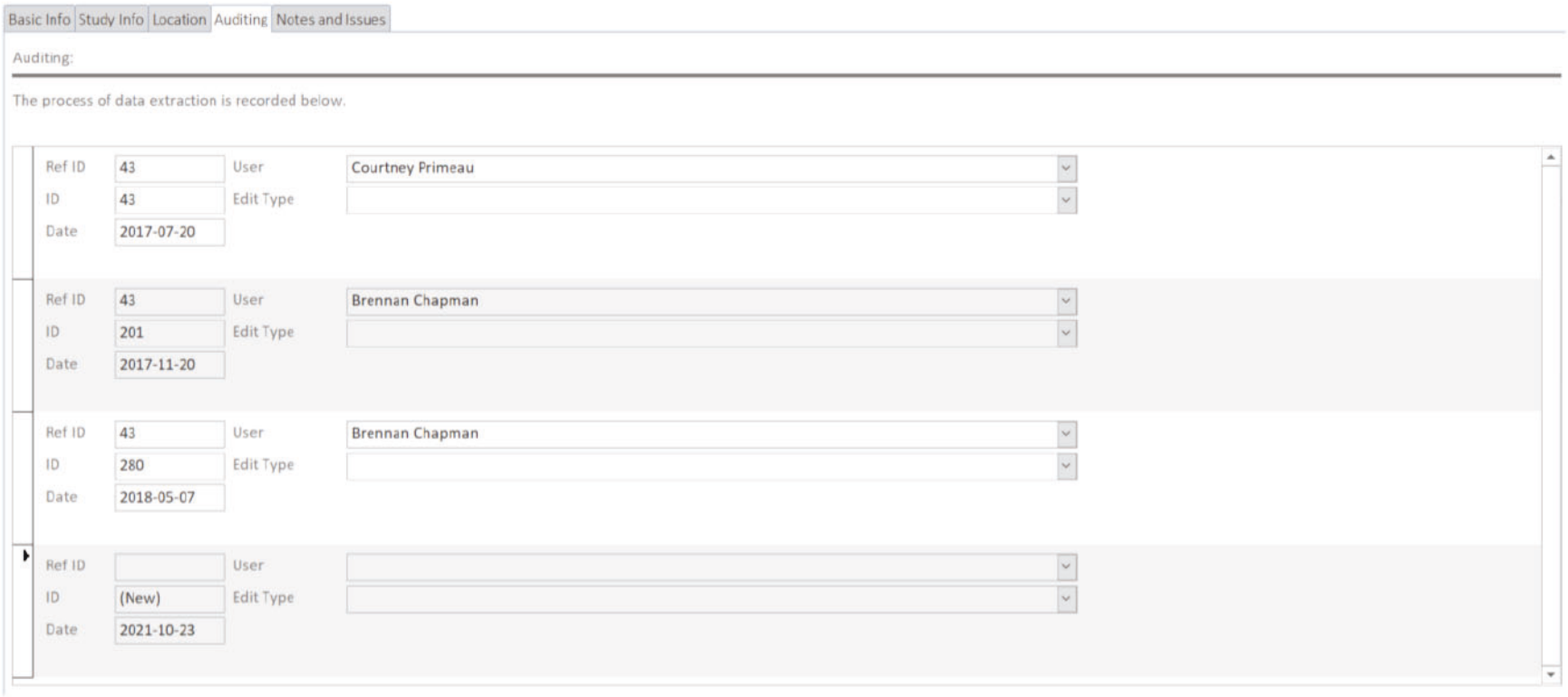
Sampling Method: Fecal samples were obtained by rectal swab of each steer on 11 occasions throughout the feeding period. This paper presents analysis of isolates collected on 5 of the 11 sampling days. The four samplings were chosen to represent the five phases in the feeding trial: (i) during their first exposure (while being fed silage-based diet); (ii) during the first period of withdrawal of antibiotics (while being fed silage-based diet); (iii) during the second exposure to antibiotics (while fed grain-based diet); and (iv) following the second withdrawal (while fed grain-based diet).

Study Reporting:

Has Explicit Breakpoints? No

Has MIC Table? No


Basic Info
Study Info
Location
Auditing
Notes and Issues
Select the Study Location Below:
Country: Canada
If a more detailed location is available (e.g. state or province), select it in the 'region' field below. If multiple locations are provided, create multiple records below. If the specified location is not listed, or a more appropriate description is available (e.g. "Nationwide"), select "Other", and provide additional detail as free-text .
Ref ID 43
ISO3 ID
ID 34
Region
Alberta
Ref ID
ISO3 ID
#Name?
ID (New)
Region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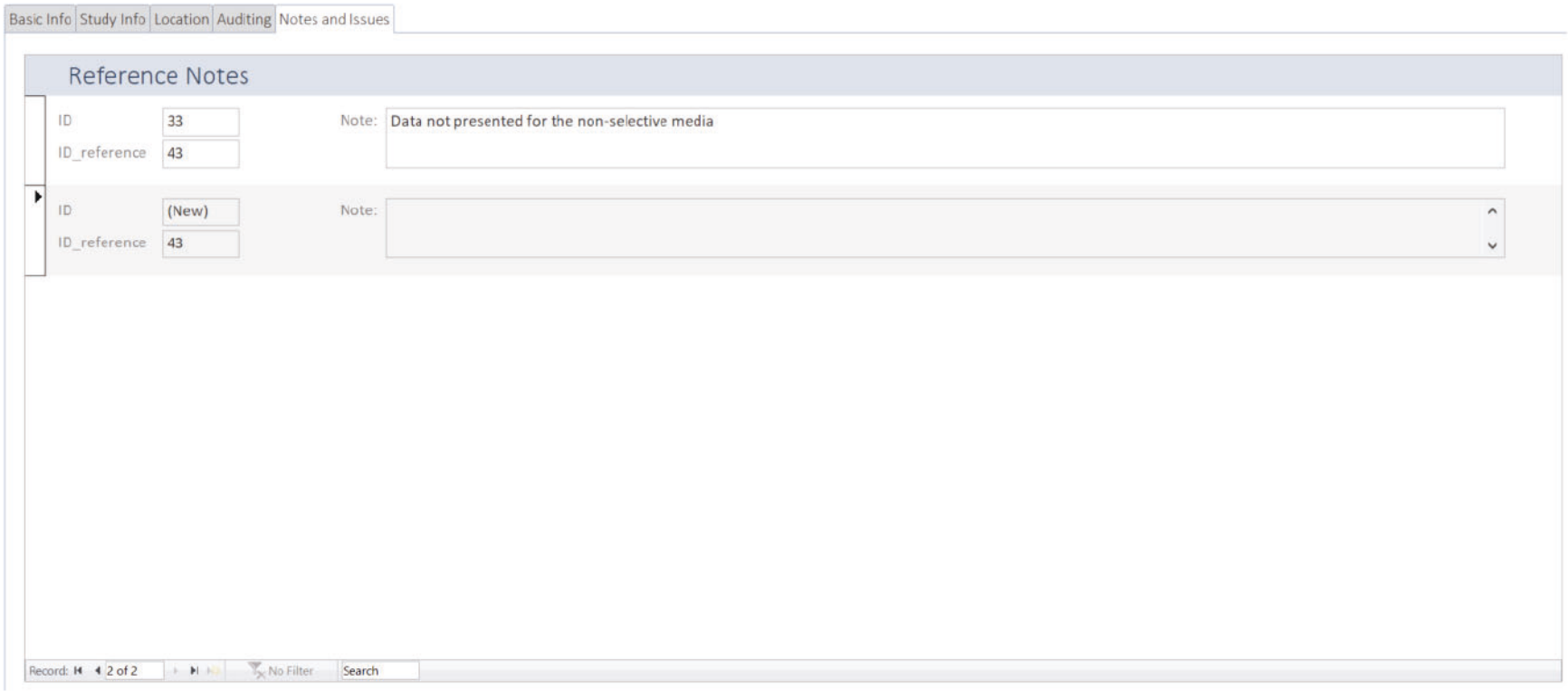
Study Info
Location
Auditing
Notes and Issues
Auditing:
The process of data extraction is recorded below.
Ref ID 43
User Courtney Primeau
ID 43
Edit Type
Date 2017-07-20
Ref ID 43
User Brennan Chapman
ID 201
Edit Type
Date 2017-11-20
Ref ID 43
User Brennan Chapman
ID 280
Edit Type
Date 2018-05-07
Ref ID
User
ID (New)
Edit Type
Date 2021-10-23

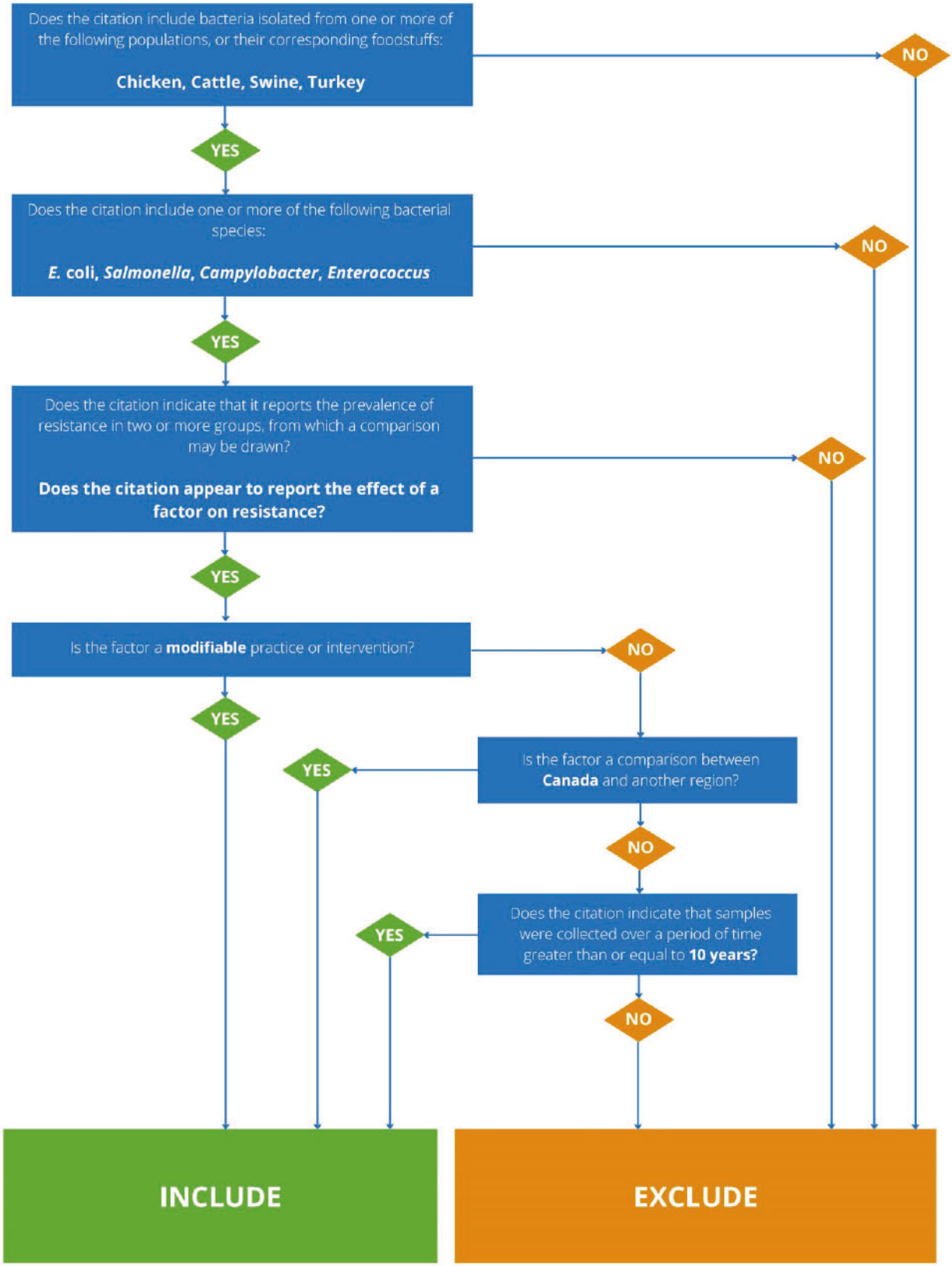

Basic Info
Study Info
Location
Auditing
Notes and Issues
Reference Notes
ID
33
ID_reference
43
Note:
Data not presented for the non-selective media
ID
(New)
ID_reference
43
Note:
Record:
2 of 2
No Filter
Search

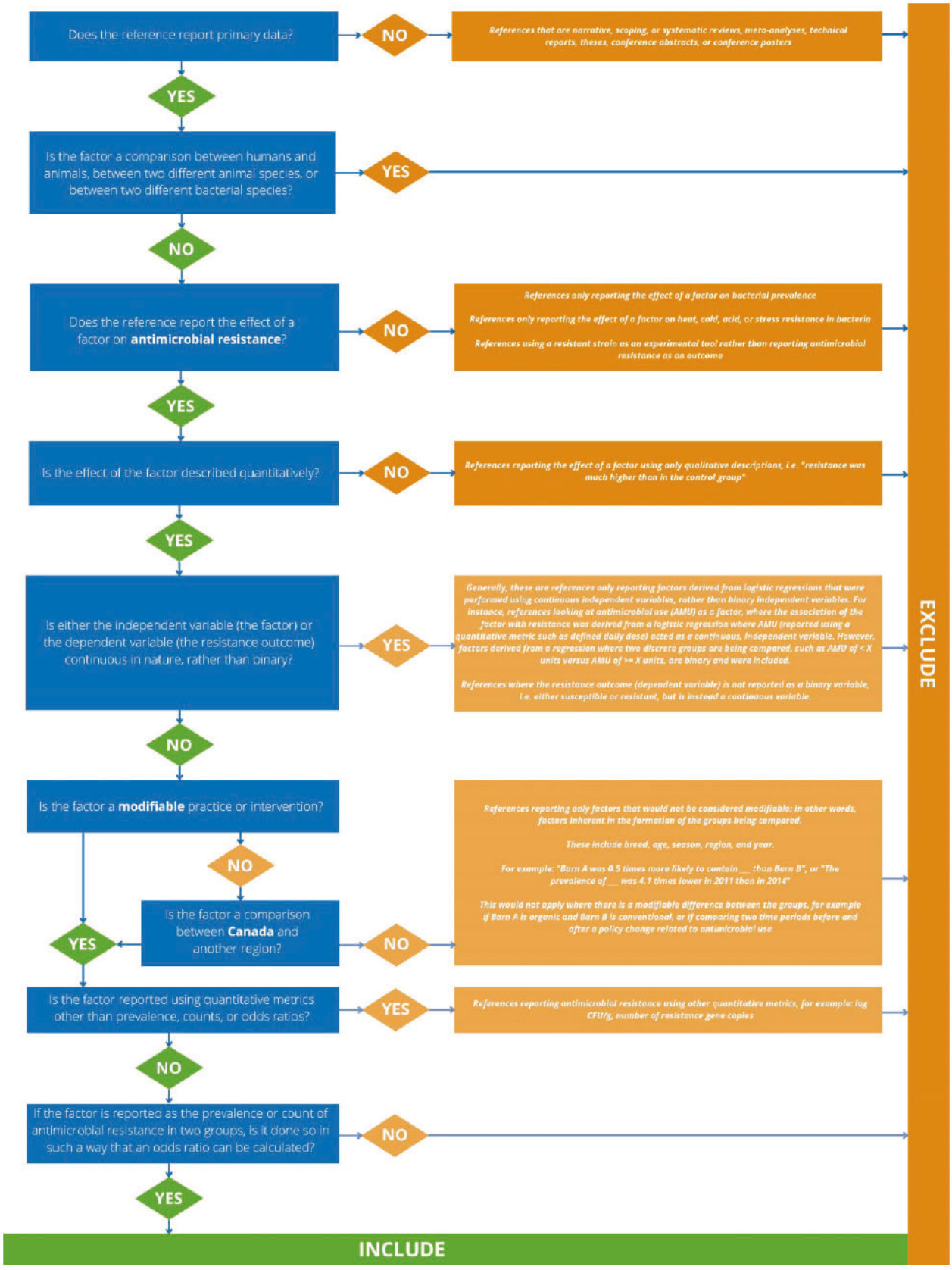

Add or Edit a Factor
00043
Open Reference
Distribution and characterization of ampicillin- and tetracycline-resistant Escherichia coli from feedlot cattle fed subtherapeutic antimicrobials
Factors
ID 532
Title
Chlortetracyline Use
Desc.
Chlortetracyline, administered in feed (days 17 - 78, 164 - 206), as Aureomycin 100-g at 11 ppm. Isolates cultured on agar amended with 4 µg/ml TET-HCL.
Duplicate Factor
Delete Factor
Host
Cattle
Microbe
Escherichia
Loc.
Table 3
Result
Contingency Table
Allocated
Observed
Stage
Farm
Farm
AMR
ampicillin
AMR +
AMR -
Total
Exposed Group
Chlortetracyline Use
2
2.7
74
Referent Group
No Use
7
6.3
111
OR
Lower
Upper
Sig.
Odds Ratio
Result or Analysis Unit
Isolate
Edit AMU
Add AMU
Delete AMU
3
chlortetracycline
ampicillin - resistance
Search ATCvet Codes
ID 533
Title
Chlortetracycline and Sulfamethazine Use
Desc.
Chlortetracycline and sulfamethazine, administered in feed (days 17 - 78, 164 - 206), as Aureo S-700G at 44 ppm. Isolates cultured on agar amended with 4 µg/ml TET-HCL.
Duplicate Factor
Delete Factor
Host
Cattle
Microbe
Escherichia
Loc.
Table 3
Result
Contingency Table
Allocated
Observed
Stage
Farm
Farm
AMR
ampicillin
AMR +
AMR -
Total
Exposed Group
Chlortetracycline + sulfamethazine Use
20
18.7
107
Referent Group
No Use
7
6.3
111
OR
Lower
Upper
Sig.
Odds Ratio
Result or Analysis Unit
Isolate
Edit AMU
Add AMU
Delete AMU
3
chlortetracycline
ampicillin - resistance
Search ATCvet Codes
ID 534
Title
Virginiamycin Use
Host
Cattle
Microbe
Escherichia
Loc.
Table 3
AMR +
AMR -
Total
Exposed Group
Virginiamycin Use
9
13
69
Referent Group
No Use
7
111
Edit AMU
Add AMU
Delete AMU
3
chlortetracycline
Record: H
1 of 24
No Filter
Search

APPENDIX 3.3

Decision Trees for the iAM.AMR Literature Screening

[In the following pages]


Does the citation include bacteria isolated from one or more of the following populations, or their corresponding foodstuffs:
Chicken, Cattle, Swine, Turkey
NO
YES
Does the citation include one or more of the following bacterial species:
E. coli, Salmonella, Campylobacter, Enterococcus
NO
YES
Does the citation indicate that it reports the prevalence of resistance in two or more groups, from which a comparison may be drawn?
Does the citation appear to report the effect of a factor on resistance?
NO
YES
Is the factor a modifiable practice or intervention?
NO
YES
Is the factor a comparison between Canada and another region?
YES
NO
Does the citation indicate that samples were collected over a period of time greater than or equal to 10 years?
YES
NO
INCLUDE
EXCLUDE


Does the reference report primary data?
NO
References that are narrative, scoping, or systematic reviews, meta-analyses, technical reports, theses, conference abstracts, or conference posters
YES
Is the factor a comparison between humans and animals, between two different animal species, or between two different bacterial species?
YES
NO
Does the reference report the effect of a factor on antimicrobial resistance?
NO
References only reporting the effect of a factor on bacterial prevalence
References only reporting the effect of a factor on heat, cold, acid, or stress resistance in bacteria
References using a resistant strain as an experimental tool rather than reporting antimicrobial resistance as an outcome
YES
Is the effect of the factor described quantitatively?
NO
References reporting the effect of a factor using only qualitative descriptions, i.e. "resistance was much higher than in the control group"
YES
Is either the independent variable (the factor) or the dependent variable (the resistance outcome) continuous in nature, rather than binary?
YES
Generally, these are references only reporting factors derived from logistic regressions that were performed using continuous independent variables, rather than binary independent variables. For instance, references looking at antimicrobial use (AMU) as a factor, where the association of the factor with resistance was derived from a logistic regression where AMU (reported using a quantitative metric such as defined daily dose) acted as a continuous, independent variable. However, factors derived from a regression where two discrete groups are being compared, such as AMU of < X units versus AMU of >= X units, are binary and were included.
References where the resistance outcome (dependent variable) is not reported as a binary variable, i.e. either susceptible or resistant, but is instead a continuous variable.
NO
Is the factor a modifiable practice or intervention?
NO
Is the factor a comparison between Canada and another region?
YES
NO
References reporting only factors that would not be considered modifiable: in other words, factors inherent in the formation of the groups being compared.
These include breed, age, season, region, and year.
For example: "Barn A was 0.5 times more likely to contain ___ than Barn B", or "The prevalence of ___ was 4.1 times lower in 2011 than in 2014"
This would not apply where there is a modifiable difference between the groups, for example if Barn A is organic and Barn B is conventional, or if comparing two time periods before and after a policy change related to antimicrobial use
YES
Is the factor reported using quantitative metrics other than prevalence, counts, or odds ratios?
YES
References reporting antimicrobial resistance using other quantitative metrics, for example: log CFU/g, number of resistance gene copies
NO
If the factor is reported as the prevalence or count of antimicrobial resistance in two groups, is it done so in such a way that an odds ratio can be calculated?
NO
YES
INCLUDE
EXCLUDE

APPENDIX 3.4

Determining the Baseline Probability of Antimicrobial Resistant *Campylobacter*

[In the following pages]

APPENDIX 3.4 Determining the baseline probability of antimicrobial resistant *Campylobacter* spp.

The lack of pre-placement data for broiler chicken from CIPARS or other surveillance program meant we needed to model the baseline prevalence of antimicrobial for the drug classes in a different way. Research suggests that there is a lag period in that newly hatched chicks appear to be free from colonization with *Campylobacter* and that most flocks become infected around 2 to 3 weeks after chick placement (1). While the reason for this lag is still under debate, the key takeaway is that if the chicks do not have *Campylobacter* at placement, then they cannot have antimicrobial resistant *Campylobacter*. After confirming with industry experts, it was decided to use this information and model the new baseline with a Pert distribution with the minimum proportion of resistant *Campylobacter* and most likely proportion of resistant *Campylobacter* both set at zero. To determine the maximum proportion at pre-placement for the Pert distribution there were only two sources of potential Canadian data, Agunos et al., 2018 (2) and 2018 CIPARS data (3).

Recall that the 2018 CIPARS data only contained pre-harvest data for *Campylobacter* in broiler chicken, but it did provide data for the four antimicrobial classes of interest (3). The Agunos et al. 2018 data included historical samples from CIPARS and assessed their susceptibility (2).

Fortunately, there were pre-placement broiler chicken samples among these samples, but unfortunately only two were positive for *Campylobacter* (2). Furthermore, one sample was not viable for susceptibility testing. The only available pre-placement *Campylobacter* sample was tested to be susceptible to all antimicrobials of interest (2). However, since this is to inform a maximum proportion, the decision was made to assume that the lost sample was

resistant to all antimicrobials of interest. Since neither source of data was ideal, it was decided to combine the data to form the maximum. Figure 3.2 is a diagram of the process used to create the baseline.

To combine these proportions, both data sets were fitted with a beta distribution where:

n=the number of samples positive for *Campylobacter* spp.

x=number of *Campylobacter* spp. samples positive for resistance to the antimicrobials of interest

$\alpha=(x+1)$

$\beta=(n.x+1)$

Then these two maximum options were combined using a Bernoulli distribution where:

p=0.5 for the maximum from Agunos et al., 2018

$(1-p)$=0.5 for the maximum from CIPARS 2018

REFERENCES

1. Newell DG, Fearnley C. Sources of *Campylobacter* Colonization in Broiler Chickens. Applied and Environmental Microbiology. 2003;69(8):4343-51.

2. Agunos A, Arsenault RK, Avery BP, Deckert AE, Gow SP, Janecko N, et al. Changes in antimicrobial resistance levels among *Escherichia coli*, *Salmonella*, and *Campylobacter* in Ontario broiler chickens between 2003 and 2015. The Canadian Journal of Veterinary Research. 2018;82(1928-9022 (Electronic)):163-77.

3. Government of Canada. Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) 2018: Figures and tables. Guelph, Ontario; 2020.

APPENDIX 3.5

Full Extracted Data Tables for the iAM.AMR *Campylobacter* Broiler Chicken Model

[In the following pages]

Paper Ref	Factor identifier in Analytica	ID	Study Country	Year	Antimicrobial Resistance	Factor Title	Factor Description
Heuer, 2001	R13950_Production_ty	1	Denmark	2001	enrofloxacin	Production type	Production type
Heuer, 2001	R13956_Production_ty	2	Denmark	2001	enrofloxacin	Production type	Production type
Meta-analysis	M00001_Production_ty	3			Fluoroquinolone	Production type	A random effects meta-analysis of outcomes described in Heuer_2001_LeinApMi related to Production type. The outcome of interest is Fluoroquinolone resistance of Campylobacter in Chicken.
Heuer, 2001	R13949_Production_ty	4	Denmark	2001	erythromycin	Production type	Production type
Heuer, 2001	R13955_Production_ty	5	Denmark	2001	erythromycin	Production type	Production type
Meta-analysis	M00002_Production_ty	6			Macrolide	Production type	A random effects meta-analysis of outcomes described in Heuer_2001_LeinApMi related to Production type. The outcome of interest is Macrolide resistance of Campylobacter in Chicken.
Heuer, 2001	R13947_Production_ty	7	Denmark	2001	tetracycline	Production type	Production type
Heuer, 2001	R13953_Production_ty	8	Denmark	2001	tetracycline	Production type	Production type
Meta-analysis	M00003_Production_ty	9			Tetracycline	Production type	A random effects meta-analysis of outcomes described in Heuer_2001_LeinApMi related to Production type. The outcome of interest is Tetracycline resistance of Campylobacter in Chicken.
Heuer, 2001	R13939_Production_ty	10	Denmark	2001	enrofloxacin	Production type	Production type
Heuer, 2001	R13944_Production_ty	11	Denmark	2001	enrofloxacin	Production type	Production type
Meta-analysis	M00004_Production_ty	12			Fluoroquinolone	Production type	A random effects meta-analysis of outcomes described in Heuer_2001_LeinApMi related to Production type. The outcome of interest is Fluoroquinolone resistance of Campylobacter in Chicken.
Heuer, 2001	R13938_Production_ty	13	Denmark	2001	erythromycin	Production type	Production type
Heuer, 2001	R13943_Production_ty	14	Denmark	2001	erythromycin	Production type	Production type
Meta-analysis	M00005_Production_ty	15			Macrolide	Production type	A random effects meta-analysis of outcomes described in Heuer_2001_LeinApMi related to Production type. The outcome of interest is Macrolide resistance of Campylobacter in Chicken.
Heuer, 2001	R13936_Production_ty	16	Denmark	2001	tetracycline	Production type	Production type
Heuer, 2001	R13941_Production_ty	17	Denmark	2001	tetracycline	Production type	Production type
Meta-analysis	M00006_Production_ty	18			Tetracycline	Production type	A random effects meta-analysis of outcomes described in Heuer_2001_LeinApMi related to Production type. The outcome of interest is Tetracycline resistance of Campylobacter in Chicken.
Adiguzel, 2018	R13692_Production_Ty	19	Turkey	2018	ciprofloxacin	Production Type	Organic vs Conventional
Bester, 2012	R13459_Production_Ty	20	South Africa	2012	ciprofloxacin	Production Type	Commercial free-range broilers were sampled from a single in-house abattoir (5-8 weeks old). Samples from industrialized chickens (5-8 weeks old) were collected from 4 abattoirs. Antibiotics are utilized therapeutically and prophylactically in both groups

Paper Ref	Factor identifier in Analytica	ID	Study Country	Year	Antimicrobial Resistance	Factor Title	Factor Description
Heuer, 2001	R139391_Production_ty	21	Denmark	2001	enrofloxacin	Production type	Production type
Heuer, 2001	R139441_Production_ty	22	Denmark	2001	enrofloxacin	Production type	Production type
Luangtongkum, 2006	R20205_Production_ty	23	United States	2006	ciprofloxacin	Production type	Resistance rates of campylobacter strains isolated from conventional vs organic farms broken down by antimicrobial agent. The whole intestinal tract was removed for testing at the abattoir and the origin of the animals was traced
Luangtongkum, 2006	R20206_Production_ty	24	United States	2006	norfloxacin	Production type	Resistance rates of campylobacter strains isolated from conventional vs organic farms broken down by antimicrobial agent. The whole intestinal tract was removed for testing at the abattoir and the origin of the animals was traced
Meta-analysis	M00007_Production_Ty	25			Fluoroquinolone	Production Type	A random effects meta-analysis of outcomes described in Adiguzel_2018_JoofVeRe.P, Bester_2012_JoofFoPr, Heuer_2001_LeinApMi, Luangtongkum2006 related to Production Type. The outcome of interest is Fluoroquinolone resistance of Campylobacter in Chicken.
Bester, 2012	R13513_Production_Ty	26	South Africa	2012	erythromycin	Production Type	Commercial free-range broilers were sampled from a single in-house abattoir (5-8 weeks old). Samples from industrialized chickens (5-8 weeks old) were collected from 4 abattoirs. Antibiotics are utilized therapeutically and prophylactically in both groups
Heuer, 2001	R139381_Production_ty	27	Denmark	2001	erythromycin	Production type	Production type
Heuer, 2001	R139431_Production_ty	28	Denmark	2001	erythromycin	Production type	Production type
Luangtongkum, 2006	R20204_Production_ty	29	United States	2006	erythromycin	Production type	Resistance rates of campylobacter strains isolated from conventional vs organic farms broken down by antimicrobial agent. The whole intestinal tract was removed for testing at the abattoir and the origin of the animals was traced
Meta-analysis	M00008_Production_Ty	30			Macrolide	Production Type	A random effects meta-analysis of outcomes described in Bester_2012_JoofFoPr, Heuer_2001_LeinApMi, Luangtongkum2006 related to Production Type. The outcome of interest is Macrolide resistance of Campylobacter in Chicken.
Adiguzel, 2018	R13693_Production_Ty	31	Turkey	2018	nalidixic acid	Production Type	Organic vs Conventional
Luangtongkum, 2006	R20207_Production_ty	32	United States	2006	nalidixic acid	Production type	Resistance rates of campylobacter strains isolated from conventional vs organic farms broken down by antimicrobial agent. The whole intestinal tract was removed for testing at the abattoir and the origin of the animals was traced

Paper Ref	Factor identifier in Analytica	ID	Study Country	Year	Antimicrobial Resistance	Factor Title	Factor Description
Meta-analysis	M00009_Production_Ty	33			Quinolone	Production Type	A random effects meta-analysis of outcomes described in Adiguzel_2018_JoofVeRe.P, Luangtongkum2006 related to Production Type. The outcome of interest is Quinolone resistance of Campylobacter in Chicken.
Adiguzel, 2018	R13691_Production_Ty	34	Turkey	2018	tetracycline	Production Type	Organic vs Conventional
Bester, 2012	R13512_Production_Ty	35	South Africa	2012	tetracycline	Production Type	Commercial free-range broilers were sampled from a single in-house abattoir (5-8 weeks old). Samples from industrialized chickens (5-8 weeks old) were collected from 4 abattoirs. Antibiotics are utilized therapeutically and prophylactically in both groups
Heuer, 2001	R139361_Production_ty	36	Denmark	2001	tetracycline	Production type	Production type
Heuer, 2001	R139411_Production_ty	37	Denmark	2001	tetracycline	Production type	Production type
Luangtongkum, 2006	R20200_Production_ty	38	United States	2006	tetracycline	Production type	Resistance rates of campylobacter strains isolated from conventional vs organic farms broken down by antimicrobial agent. The whole intestinal tract was removed for testing at the abattoir and the origin of the animals was traced
Meta-analysis	M00010_Production_Ty	39			Tetracycline	Production Type	A random effects meta-analysis of outcomes described in Adiguzel_2018_JoofVeRe.P, Bester_2012_JoofFoPr, Heuer_2001_LeinApMi, Luangtongkum2006 related to Production Type. The outcome of interest is Tetracycline resistance of Campylobacter in Chicken.
Humphrey, 2005	R20003_Difloxacin_Us	40	United Kingdom	2005	ciprofloxacin	Difloxacin Use	Flock 1 500 broilers, barn-reared treated with difloxacin (After=two weeks post treatment)
Humphrey, 2005	R20004_Difloxacin_Us	41	United Kingdom	2005	ciprofloxacin	Difloxacin Use	Flock 3 300 broilers, free-range, treated with difloxacin (After=two weeks post treatment)
Humphrey, 2005	R20005_Difloxacin_Us	42	United Kingdom	2005	ciprofloxacin	Difloxacin Use	Flock4 20,000 broilers treated with difloxacin (After=two weeks post treatment)
Humphrey, 2005	R20006_Difloxacin_Us	43	United Kingdom	2005	ciprofloxacin	Difloxacin Use	Flock 5, 1250 free-range birds (After=two weeks post treatment)
Humphrey, 2005	R20009_Enrofloxacin_	44	United Kingdom	2005	ciprofloxacin	Enrofloxacin Use	Flock 6, 5000 free-range birds (After=two weeks post treatment)
Meta-analysis	M00021_Difloxacin_Us	45			Fluoroquinolone	Difloxacin Use	A random effects meta-analysis of outcomes described in Humphrey2005, Takahashi2005 related to Difloxacin Use. The outcome of interest is Fluoroquinolone resistance of Campylobacter in Chicken.

Paper Ref	Factor identifier in Analytica	ID	Study Country	Year	Antimicrobial Resistance	Factor Title	Factor Description
Takahashi, 2005	R203410_Enrofloxacin_	46	Japan	2005	enrofloxacin	Enrofloxacin use	(study 2) 10^7 and 10&8 cfu/ml dose of C. jejuni ATCC 33560T at 18 and 23 days old and then 50 ppm enrofloxacin on day 32 vs control (between groups)
Takahashi, 2005	R203610_Enrofloxacin_	47	Japan	2005	enrofloxacin	Enrofloxacin use	(study 2) 10^7 and 10^8 cfu/ml dose of C. jejuni ATCC 33560T at 18 and 23 days old and then after 50 ppm enrofloxacin on day 32 (within groups)
Takahashi, 2005	R203620_Enrofloxacin_	48	Japan	2005	enrofloxacin	Enrofloxacin use	(study 1) 10^6 cfu/ml dose of C. jejuni ATCC 33560T at 17 daysold and then 50 ppm enrofloxacin on day 24 vs control (between groups)
Takahashi, 2005	R203630_Enrofloxacin_	49	Japan	2005	enrofloxacin	Enrofloxacin use	(study 1) 10^6 cfu/ml dose of C. jejuni ATCC 33560T at 17 daysold and then 50 ppm enrofloxacin on day 24, pre and post enrofloxacin (within groups)
Meta-analysis	M00022_Enrofloxacin_	50			Fluoroquinolone	Enrofloxacin use	A random effects meta-analysis of outcomes described in Takahashi2005 related to Enrofloxacin use. The outcome of interest is Fluoroquinolone resistance of Campylobacter in Chicken.
Takahashi, 2005	R20341_Enrofloxacin_	51	Japan	2005	enrofloxacin	Enrofloxacin use	(study 2) 10^7 and 10&8 cfu/ml dose of C. jejuni ATCC 33560T at 18 and 23 days old and then 50 ppm enrofloxacin on day 32 vs control (between groups)
Takahashi, 2005	R20361_Enrofloxacin_	52	Japan	2005	enrofloxacin	Enrofloxacin use	(study 2) 10^7 and 10^8 cfu/ml dose of C. jejuni ATCC 33560T at 18 and 23 days old and then after 50 ppm enrofloxacin on day 32 (within groups)
Takahashi, 2005	R20362_Enrofloxacin_	53	Japan	2005	enrofloxacin	Enrofloxacin use	(study 1) 10^6 cfu/ml dose of C. jejuni ATCC 33560T at 17 daysold and then 50 ppm enrofloxacin on day 24 vs control (between groups)
Takahashi, 2005	R20363_Enrofloxacin_	54	Japan	2005	enrofloxacin	Enrofloxacin use	(study 1) 10^6 cfu/ml dose of C. jejuni ATCC 33560T at 17 daysold and then 50 ppm enrofloxacin on day 24, pre and post enrofloxacin (within groups)
Jacobs-Reitsma, 1994	R13903_Flumequine_Us	55	Netherlands, The	1994	nalidixic acid	Flumequine Use	Tx group challenged with Camp. Jejuni on day 19. Tx with 15ppm flumequine on days 26-29. Sampling on day 33. Control group also challenged on day 19 but received no tx.
Jacobs-Reitsma, 1994	R13904_Flumequine_Us	56	Netherlands, The	1994	flumequine	Flumequine Use	Tx group challenged with Camp. Jejuni on day 19. Tx with 15ppm flumequine on days 26-29. Sampling on day 33. Control group also challenged on day 19 but received no tx.
Jacobs-Reitsma, 1994	R13907_Flumequine_Us	57	Netherlands, The	1994	nalidixic acid	Flumequine Use	Tx group challenged with Camp. Jejuni on day 19. Tx with 50ppm flumequine on days 26-29. Sampling on day 33. Control group also challenged on day 19 but received no tx.

Paper Ref	Factor identifier in Analytica	ID	Study Country	Year	Antimicrobial Resistance	Factor Title	Factor Description
Jacobs-Reitsma, 1994	R13908_Flumequine_Us	58	Netherlands, The	1994	flumequine	Flumequine Use	Tx group challenged with Camp. Jejuni on day 19. Tx with 50ppm flumequine on days 26-29. Sampling on day 33. Control group also challenged on day 19 but received no tx.
Meta-analysis	M00023_Flumequine_Us	59			Quinolone	Flumequine Use	A random effects meta-analysis of outcomes described in Jacobs.Reitsma_1994_LeinApMi related to Flumequine Use. The outcome of interest is Quinolone resistance of Campylobacter in Chicken.
Jacobs-Reitsma, 1994	R13911_Enrofloxacin_	60	Netherlands, The	1994	nalidixic acid	Enrofloxacin Use	Tx group challenged with Camp. Jejuni on day 19. Tx with 15ppm enrofloxacin on days 26-29. Sampling on day 33. Control group also challenged on day 19 but received no tx.
Jacobs-Reitsma, 1994	R13912_Enrofloxacin_	61	Netherlands, The	1994	flumequine	Enrofloxacin Use	Tx group challenged with Camp. Jejuni on day 19. Tx with 15ppm enrofloxacin on days 26-29. Sampling on day 33. Control group also challenged on day 19 but received no tx.
Jacobs-Reitsma, 1994	R13915_Enrofloxacin_	62	Netherlands, The	1994	nalidixic acid	Enrofloxacin Use	Tx group challenged with Camp. Jejuni on day 19. Tx with 50ppm enrofloxacin on days 26-29. Sampling on day 33. Control group also challenged on day 19 but received no tx.
Jacobs-Reitsma, 1994	R13916_Enrofloxacin_	63	Netherlands, The	1994	flumequine	Enrofloxacin Use	Tx group challenged with Camp. Jejuni on day 19. Tx with 50ppm enrofloxacin on days 26-29. Sampling on day 33. Control group also challenged on day 19 but received no tx.
Jacobs-Reitsma, 1994	R13920_Enrofloxacin_	64	Netherlands, The	1994	nalidixic acid	Enrofloxacin Use	Tx group challenged with Camp. Jejuni on day 19. Tx with 50ppm enrofloxacin on days 1-4. Sampling on day 33. Control group also challenged on day 19 but received no tx.
Jacobs-Reitsma, 1994	R13921_Enrofloxacin_	65	Netherlands, The	1994	flumequine	Enrofloxacin Use	Tx group challenged with Camp. Jejuni on day 19. Tx with 50ppm enrofloxacin on days 1-4. Sampling on day 33. Control group also challenged on day 19 but received no tx.
Meta-analysis	M00024_Enrofloxacin_	66			Quinolone	Enrofloxacin Use	A random effects meta-analysis of outcomes described in Jacobs.Reitsma_1994_LeinApMi related to Enrofloxacin Use. The outcome of interest is Quinolone resistance of Campylobacter in Chicken.
Jacobs-Reitsma, 1994	R13905_Flumequine_Us	67	Netherlands, The	1994	enrofloxacin	Flumequine Use	Tx group challenged with Camp. Jejuni on day 19. Tx with 15ppm flumequine on days 26-29. Sampling on day 33. Control group also challenged on day 19 but received no tx.
Jacobs-Reitsma, 1994	R13909_Flumequine_Us	68	Netherlands, The	1994	enrofloxacin	Flumequine Use	Tx group challenged with Camp. Jejuni on day 19. Tx with 50ppm flumequine on days 26-29. Sampling on day 33. Control group also challenged on day 19 but received no tx.

Paper Ref	Factor identifier in Analytica	ID	Study Country	Year	Antimicrobial Resistance	Factor Title	Factor Description
Meta-analysis	M00025_Flumequine_Us	69			Fluoroquinolone	Flumequine Use	A random effects meta-analysis of outcomes described in Jacobs.Reitsma_1994_LeinApMi related to Flumequine Use. The outcome of interest is Fluoroquinolone resistance of Campylobacter in Chicken.
Jacobs-Reitsma, 1994	R13913_Enrofloxacin_	70	Netherlands, The	1994	enrofloxacin	Enrofloxacin Use	Tx group challenged with Camp. Jejuni on day 19. Tx with 15ppm enrofloxacin on days 26-29. Sampling on day 33. Control group also challenged on day 19 but received no tx.
Jacobs-Reitsma, 1994	R13917_Enrofloxacin_	71	Netherlands, The	1994	enrofloxacin	Enrofloxacin Use	Tx group challenged with Camp. Jejuni on day 19. Tx with 50ppm enrofloxacin on days 26-29. Sampling on day 33. Control group also challenged on day 19 but received no tx.
Jacobs-Reitsma, 1994	R13922_Enrofloxacin_	72	Netherlands, The	1994	enrofloxacin	Enrofloxacin Use	Tx group challenged with Camp. Jejuni on day 19. Tx with 50ppm enrofloxacin on days 1-4. Sampling on day 33. Control group also challenged on day 19 but received no tx.
McDermott, 2002	R20092_Sarafloxacin_	73	United States	2002	ciprofloxacin	Sarafloxacin Use	Experimental groups of sarafloxacin use compared to non-medicated controls for ciprofloxacin resistance. *figure extraction using plotdigitizer*
Meta-analysis	M00026_Enrofloxacin_	74			Fluoroquinolone	Enrofloxacin Use	A random effects meta-analysis of outcomes described in Jacobs.Reitsma_1994_LeinApMi, McDermott2002 related to Enrofloxacin Use. The outcome of interest is Fluoroquinolone resistance of Campylobacter in Chicken.
Meta-analysis	M00031_Meat_chilling	75			Fluoroquinolone	Meat chilling type	A random effects meta-analysis of outcomes described in Sanchez2002 related to Meat chilling type. The outcome of interest is Fluoroquinolone resistance of Campylobacter in Chicken.
Sanchez, 2002	R20320_Meat_chilling	76	United States	2002	ciprofloxacin	Meat chilling type	Whole-carcass broilers processed in immersion-chilling vs air-chilling (*cephalothin is the spelling used in the paper)
Sanchez, 2002	R20321_Meat_chilling	77	United States	2002	enrofloxacin	Meat chilling type	Whole-carcass broilers processed in immersion-chilling vs air-chilling (*cephalothin is the spelling used in the paper)
Sanchez, 2002	R20322_Meat_chilling	78	United States	2002	grepafloxacin	Meat chilling type	Whole-carcass broilers processed in immersion-chilling vs air-chilling (*cephalothin is the spelling used in the paper)
Sanchez, 2002	R20323_Meat_chilling	79	United States	2002	levofloxacin	Meat chilling type	Whole-carcass broilers processed in immersion-chilling vs air-chilling (*cephalothin is the spelling used in the paper)
Adiguzel, 2018	R13696_Production_Ty	80	Turkey	2018	erythromycin	Production Type	Organic vs Conventional
Asai, 2007	R11808_Fluoroquinolo	81	Japan	2007	enrofloxacin	Fluoroquinolone Use	Fluoroquinolone Use in the Past 6 Months
Asai, 2007	R11809_Tetracycline_	82	Japan	2007	oxytetracycline	Tetracycline Use	Tetracycline Use in the Past 6 Months
Asai, 2007	R12748_Fluoroquinolo	83	Japan	2007	enrofloxacin	Fluoroquinolone Use	Fluoroquinolone Use in the Past 6 Months
Asai, 2007	R12752_Tetracycline_	84	Japan	2007	oxytetracycline	Tetracycline Use	Tetracycline Use in the Past 6 Months

Paper Ref	Factor identifier in Analytica	ID	Study Country	Year	Antimicrobial Resistance	Factor Title	Factor Description
Avrain, 2003	R11810_Avilamycin_Us	85	France	2003	tetracycline	Avilamycin Use	Avilamycin use in standard (conventional) production.
Avrain, 2003	R12023_Tetracycline_	86	France	2003	enrofloxacin	Tetracycline Use	Tetracycline use in export production.
Avrain, 2003	R12909_Ionophore_Use	87	France	2003	nalidixic acid	Ionophore Use	Ionophone use in standard (conventional) production.
Hoogenboom, 2008	R30197_Production_ty	88	Netherlands, The	2008	ciprofloxacin	Production type	Production type
Hoogenboom, 2008	R30198_Production_ty	89	Netherlands, The	2008	doxycycline	Production type	Production type
Hoogenboom, 2008	R30199_Production_ty	90	Netherlands, The	2008	erythromycin	Production type	Production type
Hoogenboom, 2008	R30202_Production_ty	91	Netherlands, The	2008	nalidixic acid	Production type	Production type
Ladely, 2007	R20025_Tylosin_Use	92	United States	2007	erythromycin	Tylosin Use	Distribution of erythromycin resistance for C. jejuni and C. coli recovered from ceca receiving either subtherapeutic (22 ppm of tylosin phosphate) or therapeutic (529 ppm of tylosin tartrate) concentrations of tylosin. Using week 6 age.
Ladely, 2007	R200250_Tylosin_Use	93	United States	2007	erythromycin	Tylosin Use	Distribution of erythromycin resistance for C. jejuni and C. coli recovered from ceca receiving either subtherapeutic (22 ppm of tylosin phosphate) or therapeutic (529 ppm of tylosin tartrate) concentrations of tylosin. Using week 6 age.
Ladely, 2007	R200251_Tylosin_Use	94	United States	2007	erythromycin	Tylosin Use	Distribution of erythromycin resistance for C. jejuni and C. coli recovered from ceca receiving either subtherapeutic (22 ppm of tylosin phosphate) or therapeutic (529 ppm of tylosin tartrate) concentrations of tylosin. Using week 6 age.
Sanchez, 2002	R20319_Meat_chilling	95	United States	2002	nalidixic acid	Meat chilling type	Whole-carcass broilers processed in immersion-chilling vs air-chilling (*cephalothin is the spelling used in the paper)
Sanchez, 2002	R20325_Meat_chilling	96	United States	2002	erythromycin	Meat chilling type	Whole-carcass broilers processed in immersion-chilling vs air-chilling (*cephalothin is the spelling used in the paper)
Sanchez, 2002	R20326_Meat_chilling	97	United States	2002	tetracycline	Meat chilling type	Whole-carcass broilers processed in immersion-chilling vs air-chilling (*cephalothin is the spelling used in the paper)
Soonthornchaikul, 2006	R20331_Packaging_typ	98	United Kingdom	2006	nalidixic acid	Packaging type	Unpackaged butcher intensively-reared chicken vs pre-packaged supermarket intensively-reared chicken (chicken carcass)
Soonthornchaikul, 2006	R20332_Packaging_typ	99	United Kingdom	2006	erythromycin	Packaging type	Unpackaged butcher intensively-reared chicken vs pre-packaged supermarket intensively-reared chicken (chicken carcass)
Soonthornchaikul, 2006	R20333_Packaging_typ	100	United Kingdom	2006	ciprofloxacin	Packaging type	Unpackaged butcher intensively-reared chicken vs pre-packaged supermarket intensively-reared chicken (chicken carcass)
Stapleton, 2010	R20364_Enrofloxacin_	101	United Kingdom	2010	ciprofloxacin	Enrofloxacin use	Comparison of ciprofloxacin resistance based on amount of enrofloxacin use groups after 48 hours of use (experiment 1)

Paper Ref	Factor identifier in Analytica	ID	Study Country	Year	Antimicrobial Resistance	Factor Title	Factor Description
Stapleton, 2010	R20371_Enrofloxacin_	102	United Kingdom	2010	ciprofloxacin	Enrofloxacin use	Comparison of ciprofloxacin resistance based on amount of enrofloxacin use groups after 48 hours of use (experiment 1)
Stapleton, 2010	R20373_Enrofloxacin_	103	United Kingdom	2010	ciprofloxacin	Enrofloxacin use	Comparison of ciprofloxacin resistance based on amount of enrofloxacin use groups after 48 hours of use (experiment 2)
Stapleton, 2010	R20374_Enrofloxacin_	104	United Kingdom	2010	ciprofloxacin	Enrofloxacin use	Comparison of ciprofloxacin resistance based on amount of enrofloxacin use groups after 48 hours of use (experiment 2)

Paper Ref	ID	Exposed Group	Referent Group	Odds Ratio	Standard Error of the Log Odds Ratio	*p* value	log Odds Ratio	Meta-analysis ID	Meta-analysis Antimicrobial Class
Heuer, 2001	1	Organic production	Conventional production	0.2	1.932183566	0.466666667	-1.609437912	1	Fluoroquinolone
Heuer, 2001	2	Extensive indoor production	Conventional production	0.090909091	1.874873733	0.133333333	-2.397895273	1	Fluoroquinolone
Meta-analysis	3	Organic production or Extensive indoor production	Conventional production	0.133249361	1.345540551	0.13415	NA	1	Fluoroquinolone
Heuer, 2001	4	Organic production	Conventional production	1	2.19089023	1	0	2	Macrolide
Heuer, 2001	5	Extensive indoor production	Conventional production	1.666666667	1.813529401	1	0.510825624	2	Macrolide
Meta-analysis	6	Organic production or Extensive indoor production	Conventional production	1.35408682	1.397014084	0.828222159	NA	2	Macrolide
Heuer, 2001	7	Organic production	Conventional production	1	2.19089023	1	0	3	Tetracycline
Heuer, 2001	8	Extensive indoor production	Conventional production	0.454545455	2.140518204	1	-0.78845736	3	Tetracycline
Meta-analysis	9	Organic production or Extensive indoor production	Conventional production	0.668046973	1.531073495	0.7921859	NA	3	Tetracycline
Heuer, 2001	10	Organic production	Conventional production	0.538461538	2.036300603	1	-0.619039208	4	Fluoroquinolone
Heuer, 2001	11	Extensive indoor production	Conventional production	1.340425532	1.674651592	1	0.292987125	4	Fluoroquinolone
Meta-analysis	12	Organic production or Extensive indoor production	Conventional production	0.927760963	1.293431389	0.953771943	NA	4	Fluoroquinolone
Heuer, 2001	13	Organic production	Conventional production	0.538461538	2.036300603	1	-0.619039208	5	Macrolide
Heuer, 2001	14	Extensive indoor production	Conventional production	0.428571429	2.033729191	1	-0.84729786	5	Macrolide
Meta-analysis	15	Organic production or Extensive indoor production	Conventional production	0.480315189	1.438971972	0.610325574	NA	5	Macrolide
Heuer, 2001	16	Organic production	Conventional production	1.702702703	1.678081886	0.540229885	0.532216814	6	Tetracycline
Heuer, 2001	17	Extensive indoor production	Conventional production	0.428571429	2.033729191	1	-0.84729786	6	Tetracycline
Meta-analysis	18	Organic production or Extensive indoor production	Conventional production	0.973785034	1.29434776	0.983625669	NA	6	Tetracycline
Adiguzel, 2018	19	Organic	Conventional	0.274633124	1.641497018	0.209413495	-1.292319168	7	Fluoroquinolone
Bester, 2012	20	Commercial Free-Range	Industrial	111.3	0.684159538	3.81E-22	4.712229258	7	Fluoroquinolone
Heuer, 2001	21	Organic production	Conventional production	0.581395349	2.031381704	1	-0.542324291	7	Fluoroquinolone
Heuer, 2001	22	Extensive indoor production	Conventional production	0.392857143	1.458294681	0.504878049	-0.934309237	7	Fluoroquinolone
Luangtongkum, 2006	23	Organic	Conventional	0.00361353	1.424795829	4.35E-28	-5.623070144	7	Fluoroquinolone
Luangtongkum, 2006	24	Organic	Conventional	0.003527921	1.424779016	5.43E-29	-5.647046461	7	Fluoroquinolone

Paper Ref	ID	Exposed Group	Referent Group	Odds Ratio	Standard Error of the Log Odds Ratio	*p* value	log Odds Ratio	Meta-analysis ID	Meta-analysis Antimicrobial Class
Meta-analysis	25	Organic or Commercial Free-Range or Organic production or Extensive indoor production	Conventional or Industrial or Conventional production	0.230738707	1.671106043	0.380191145	NA	7	Fluoroquinolone
Bester, 2012	26	Commercial Free-Range	Industrial	7.975	0.453737526	1.24E-06	2.076311649	8	Macrolide
Heuer, 2001	27	Organic production	Conventional production	0.581395349	2.031381704	1	-0.542324291	8	Macrolide
Heuer, 2001	28	Extensive indoor production	Conventional production	1.315789474	1.667859222	1	0.274436846	8	Macrolide
Luangtongkum, 2006	29	Organic	Conventional	34.50166113	1.44122545	9.46E-06	3.541007472	8	Macrolide
Meta-analysis	30	Commercial Free-Range or Organic production or Extensive indoor production or Organic	Industrial or Conventional production or Conventional	7.236592594	0.410288984	1.41E-06	NA	8	Macrolide
Adiguzel, 2018	31	Organic	Conventional	11.52941176	0.636025533	3.52E-06	2.444901315	9	Quinolone
Luangtongkum, 2006	32	Organic	Conventional	0.003527921	1.424779016	5.43E-29	-5.647046461	9	Quinolone
Meta-analysis	33	Organic	Conventional	0.222988457	4.044727068	0.710629884	NA	9	Quinolone
Adiguzel, 2018	34	Organic	Conventional	4102.2	1.558230565	1.10E-39	8.319278694	10	Tetracycline
Bester, 2012	35	Commercial Free-Range	Industrial	3.192	1.642468953	0.240429338	1.16064768	10	Tetracycline
Heuer, 2001	36	Organic production	Conventional production	1.829268293	1.671959077	0.529411765	0.603916047	10	Tetracycline
Heuer, 2001	37	Extensive indoor production	Conventional production	0.423728814	2.028274711	1	-0.858661619	10	Tetracycline
Luangtongkum, 2006	38	Organic	Conventional	0.276595745	0.266094461	7.16E-07	-1.285198244	10	Tetracycline
Meta-analysis	39	Organic or Commercial Free-Range or Organic production or Extensive indoor production	Conventional or Industrial or Conventional production	4.663257197	1.758143912	0.381159882	NA	10	Tetracycline
Humphrey, 2005	40	After	Before	33	1.083624669	4.23E-04	3.496507561	21	Fluoroquinolone
Humphrey, 2005	41	After	Before	65	1.294960647	1.68E-04	4.17438727	21	Fluoroquinolone
Humphrey, 2005	42	After	Before	63	1.546458661	1.53E-04	4.143134726	21	Fluoroquinolone
Humphrey, 2005	43	After	Before	63	1.546458661	1.53E-04	4.143134726	21	Fluoroquinolone
Humphrey, 2005	44	After	Before	2.333333333	0.827359541	0.428307982	0.84729786	21	Fluoroquinolone
Meta-analysis	45	After or 50ppm enrofloxacin day 28	Before or no enrofloxacin day 28 or before 50ppm enrofloxacin	22.55552483	0.711733713	1.20E-05	NA	21	Fluoroquinolone
Takahashi, 2005	46	50ppm enrofloxacin day 28	no enrofloxacin day 28	441	2.047065263	1.08E-05	6.089044875	21	Fluoroquinolone

Paper Ref	ID	Exposed Group	Referent Group	Odds Ratio	Standard Error of the Log Odds Ratio	*p* value	log Odds Ratio	Meta-analysis ID	Meta-analysis Antimicrobial Class
Takahashi, 2005	47	50ppm enrofloxacin day 28	before 50ppm enrofloxacin	441	2.047065263	1.08E-05	6.089044875	21	Fluoroquinolone
Takahashi, 2005	48	50ppm enrofloxacin day 28	no enrofloxacin day 28	1	2.047065263	1	0	21	Fluoroquinolone
Takahashi, 2005	49	50ppm enrofloxacin day 28	before 50ppm enrofloxacin	1	2.047065263	1	0	21	Fluoroquinolone
Meta-analysis	50	50ppm enrofloxacin day 28	no enrofloxacin day 28 or before 50ppm enrofloxacin	21	1.757755849	0.083264517	NA	22	Fluoroquinolone
Takahashi, 2005	51	50ppm enrofloxacin day 28	no enrofloxacin day 28	441	2.047065263	1.08E-05	6.089044875	22	Fluoroquinolone
Takahashi, 2005	52	50ppm enrofloxacin day 28	before 50ppm enrofloxacin	441	2.047065263	1.08E-05	6.089044875	22	Fluoroquinolone
Takahashi, 2005	53	50ppm enrofloxacin day 28	no enrofloxacin day 28	1	2.047065263	1	0	22	Fluoroquinolone
Takahashi, 2005	54	50ppm enrofloxacin day 28	before 50ppm enrofloxacin	1	2.047065263	1	0	22	Fluoroquinolone
Jacobs-Reitsma, 1994	55	Flumequine use	No use	0.411764706	2.098418772	1	-0.887303195	23	Quinolone
Jacobs-Reitsma, 1994	56	Flumequine use	No use	0.411764706	2.098418772	1	-0.887303195	23	Quinolone
Jacobs-Reitsma, 1994	57	Flumequine use	No use	0.411764706	2.098418772	1	-0.887303195	23	Quinolone
Jacobs-Reitsma, 1994	58	Flumequine use	No use	0.411764706	2.098418772	1	-0.887303195	23	Quinolone
Meta-analysis	59	Flumequine use	No use	0.411764706	1.049209386	0.397727134	NA	23	Quinolone
Jacobs-Reitsma, 1994	60	Enrofloxacin use	No use	119	2.098418772	0.002020202	4.779123493	24	Quinolone
Jacobs-Reitsma, 1994	61	Enrofloxacin use	No use	119	2.098418772	0.002020202	4.779123493	24	Quinolone
Jacobs-Reitsma, 1994	62	Enrofloxacin use	No use	119	2.098418772	0.002020202	4.779123493	24	Quinolone
Jacobs-Reitsma, 1994	63	Enrofloxacin use	No use	119	2.098418772	0.002020202	4.779123493	24	Quinolone
Jacobs-Reitsma, 1994	64	Enrofloxacin use	No use	1	2.138089935	1	0	24	Quinolone
Jacobs-Reitsma, 1994	65	Enrofloxacin use	No use	1	2.138089935	1	0	24	Quinolone
Meta-analysis	66	Enrofloxacin use	No use	24.91990611	0.998015696	0.001272723	NA	24	Quinolone
Jacobs-Reitsma, 1994	67	Flumequine use	No use	0.411764706	2.098418772	1	-0.887303195	25	Fluoroquinolone

Paper Ref	ID	Exposed Group	Referent Group	Odds Ratio	Standard Error of the Log Odds Ratio	*p* value	log Odds Ratio	Meta-analysis ID	Meta-analysis Antimicrobial Class
Jacobs-Reitsma, 1994	68	Flumequine use	No use	0.411764706	2.098418772	1	-0.887303195	25	Fluoroquinolone
Meta-analysis	69	Flumequine use	No use	0.411764706	1.483806144	0.549845725	NA	25	Fluoroquinolone
Jacobs-Reitsma, 1994	70	Enrofloxacin use	No use	119	2.098418772	0.002020202	4.779123493	26	Fluoroquinolone
Jacobs-Reitsma, 1994	71	Enrofloxacin use	No use	119	2.098418772	0.002020202	4.779123493	26	Fluoroquinolone
Jacobs-Reitsma, 1994	72	Enrofloxacin use	No use	1	2.138089935	1	0	26	Fluoroquinolone
McDermott, 2002	73	Sarafloxacin Use	No use	3333	1.64519624	3.39E-27	8.111628078	26	Fluoroquinolone
Meta-analysis	74	Enrofloxacin use or Sarafloxacin Use	No use	97.34513754	1.70258266	0.007166415	NA	26	Fluoroquinolone
Meta-analysis	75	immersion-chilling	air-chilling	5.135878996	0.27290632	2.03E-09	NA	31	Fluoroquinolone
Sanchez, 2002	76	immersion-chilling	air-chilling	6.254545455	0.410282307	2.89E-06	1.833308472	31	Fluoroquinolone
Sanchez, 2002	77	immersion-chilling	air-chilling	11.45925926	1.47833274	0.032782851	2.438798072	31	Fluoroquinolone
Sanchez, 2002	78	immersion-chilling	air-chilling	7.534883721	0.524507069	2.08E-05	2.0195434	31	Fluoroquinolone
Sanchez, 2002	79	immersion-chilling	air-chilling	3.044397463	0.410282307	0.007767544	1.113303004	31	Fluoroquinolone
Adiguzel, 2018	80	Organic	Conventional	1.195488722	2.006892177	1	0.178555074	NA	NA
Asai, 2007	81	Fluoroquinolone Use	No Fluoroquinolone Use	16.35135135	1.571808824	0.060126582	2.794310545	NA	NA
Asai, 2007	82	Tetracycline Use	No Tetracycline Use	0.909090909	0.799147273	1	-0.09531018	NA	NA
Asai, 2007	83	Fluoroquinolone Use	No Fluoroquinolone Use	1.545454545	2.073515189	1	0.435318071	NA	NA
Asai, 2007	84	Tetracycline Use	No Tetracycline Use	5.909090909	1.653984382	0.472527473	1.776491997	NA	NA
Avrain, 2003	85	Avilamycin use	No Use	1.99137931	0.290911579	0.022708721	0.688827519	NA	NA
Avrain, 2003	86	Tetracycline Use	No Use	4.285714286	0.65538066	0.030033212	1.455287233	NA	NA
Avrain, 2003	87	Ionophore Use	No Use	4	0.62915287	0.039406202	1.386294361	NA	NA
Hoogenboom, 2008	88	organic	conventional	1.675362319	0.445398947	0.273371584	0.516029452	NA	NA
Hoogenboom, 2008	89	organic	conventional	0.927350427	0.444638876	1	-0.075423762	NA	NA
Hoogenboom, 2008	90	organic	conventional	1.769230769	2.012004109	1	0.570544858	NA	NA
Hoogenboom, 2008	91	organic	conventional	1.675362319	0.445398947	0.273371584	0.516029452	NA	NA
Ladely, 2007	92	Subtherapeutic	Therapeutic	12.6	1.778174559	0.065934066	2.533696814	NA	NA

Paper Ref	ID	Exposed Group	Referent Group	Odds Ratio	Standard Error of the Log Odds Ratio	*p* value	log Odds Ratio	Meta-analysis ID	Meta-analysis Antimicrobial Class
Ladely, 2007	93	Subtherapeutic	Therapeutic	13.75	0.970004686	0.006329549	2.621038824	NA	NA
Ladely, 2007	94	Subtherapeutic	Therapeutic	109.8888889	1.534825844	6.72E-07	4.699469754	NA	NA
Sanchez, 2002	95	immersion-chilling	air-chilling	10.50810811	0.522803331	2.18E-07	2.35214716	NA	NA
Sanchez, 2002	96	immersion-chilling	air-chilling	3.044397463	0.410282307	0.007767544	1.113303004	NA	NA
Sanchez, 2002	97	immersion-chilling	air-chilling	0.018214936	0.564132338	4.96E-19	-4.005513349	NA	NA
Soonthornchaikul, 2006	98	Unpackaged butcher	pre-packaged supermarket	1	2.016326802	1	0	NA	NA
Soonthornchaikul, 2006	99	Unpackaged butcher	pre-packaged supermarket	1	2.016326802	1	0	NA	NA
Soonthornchaikul, 2006	100	Unpackaged butcher	pre-packaged supermarket	3.272727273	0.735407993	0.180580404	1.185623666	NA	NA
Stapleton, 2010	101	250 ppm enrofloxacin	50 ppm enrofloxacin	1.139941691	0.267797765	0.691619983	0.130977113	NA	NA
Stapleton, 2010	102	125 ppm enrofloxacin	50 ppm enrofloxacin	1.488629738	0.200214119	0.055650976	0.397856058	NA	NA
Stapleton, 2010	103	(125 ppm and 250 ppm) enrofloxacin	12 ppm enrofloxacin	283.8732394	1.013989795	1.11E-43	5.648527799	NA	NA
Stapleton, 2010	104	(25 ppm and 50 ppm) enrofloxacin	12 ppm enrofloxacin	1.945433608	0.184111851	3.23E-04	0.665484887	NA	NA

Paper Ref	ID	Meta-Analysis Type	Host	*Campylobacter* species	Allocation Stage	Observed Stage	Unit of Sampling	Result Format	A	B	C	D
Heuer, 2001	1	Within Study, Same Antimicrobial Class	Broilers	coli	Farm	Farm	Isolate	Contingency Table	0.5	2.5	1.5	1.5
Heuer, 2001	2	Within Study, Same Antimicrobial Class	Broilers	coli	Farm	Farm	Isolate	Contingency Table	0.5	5.5	1.5	1.5
Meta-analysis	3	Within Study, Same Antimicrobial Class	Broilers	coli	Farm	NA	NA	Odds Ratio	NA	NA	NA	NA
Heuer, 2001	4	Within Study, Same Antimicrobial Class	Broilers	coli	Farm	Farm	Isolate	Contingency Table	0.5	2.5	0.5	2.5
Heuer, 2001	5	Within Study, Same Antimicrobial Class	Broilers	coli	Farm	Farm	Isolate	Contingency Table	1.5	4.5	0.5	2.5
Meta-analysis	6	Within Study, Same Antimicrobial Class	Broilers	coli	Farm	NA	NA	Odds Ratio	NA	NA	NA	NA
Heuer, 2001	7	Within Study, Same Antimicrobial Class	Broilers	coli	Farm	Farm	Isolate	Contingency Table	0.5	2.5	0.5	2.5
Heuer, 2001	8	Within Study, Same Antimicrobial Class	Broilers	coli	Farm	Farm	Isolate	Contingency Table	0.5	5.5	0.5	2.5
Meta-analysis	9	Within Study, Same Antimicrobial Class	Broilers	coli	Farm	NA	NA	Odds Ratio	NA	NA	NA	NA
Heuer, 2001	10	Within Study, Same Antimicrobial Class	Broilers	jejuni	Farm	Farm	Isolate	Contingency Table	0.5	19.5	0.5	10.5
Heuer, 2001	11	Within Study, Same Antimicrobial Class	Broilers	jejuni	Farm	Farm	Isolate	Contingency Table	1.5	23.5	0.5	10.5
Meta-analysis	12	Within Study, Same Antimicrobial Class	Broilers	jejuni	Farm	NA	NA	Odds Ratio	NA	NA	NA	NA
Heuer, 2001	13	Within Study, Same Antimicrobial Class	Broilers	jejuni	Farm	Farm	Isolate	Contingency Table	0.5	19.5	0.5	10.5
Heuer, 2001	14	Within Study, Same Antimicrobial Class	Broilers	jejuni	Farm	Farm	Isolate	Contingency Table	0.5	24.5	0.5	10.5
Meta-analysis	15	Within Study, Same Antimicrobial Class	Broilers	jejuni	Farm	NA	NA	Odds Ratio	NA	NA	NA	NA
Heuer, 2001	16	Within Study, Same Antimicrobial Class	Broilers	jejuni	Farm	Farm	Isolate	Contingency Table	1.5	18.5	0.5	10.5
Heuer, 2001	17	Within Study, Same Antimicrobial Class	Broilers	jejuni	Farm	Farm	Isolate	Contingency Table	0.5	24.5	0.5	10.5
Meta-analysis	18	Within Study, Same Antimicrobial Class	Broilers	jejuni	Farm	NA	NA	Odds Ratio	NA	NA	NA	NA
Adiguzel, 2018	19	Across Studies, Same Antimicrobial Class	Carcass	combination	Farm	Farm	Isolate	Contingency Table	65.5	1.5	79.5	0.5
Bester, 2012	20	Across Studies, Same Antimicrobial Class	Broilers	Other	Farm	Farm	Isolate	Prevalence Table	63	3	10	53
Heuer, 2001	21	Across Studies, Same Antimicrobial Class	Broilers	combination	Farm	Farm	Isolate	Contingency Table	0.5	21.5	0.5	12.5
Heuer, 2001	22	Across Studies, Same Antimicrobial Class	Broilers	combination	Farm	Farm	Isolate	Contingency Table	1	28	1	11
Luangtongkum, 2006	23	Across Studies, Same Antimicrobial Class	Carcass	Combination	Farm	Farm	Isolate	Contingency Table	0.5	165.5	76.5	91.5
Luangtongkum, 2006	24	Across Studies, Same Antimicrobial Class	Carcass	Combination	Farm	Farm	Isolate	Contingency Table	0.5	165.5	77.5	90.5
Meta-analysis	25	Across Studies, Same Antimicrobial Class	Carcass	spp.	Farm	NA	NA	Odds Ratio	NA	NA	NA	NA
Bester, 2012	26	Across Studies, Same Antimicrobial Class	Broilers	Other	Farm	Farm	Isolate	Prevalence Table	58	8	30	33
Heuer, 2001	27	Across Studies, Same Antimicrobial Class	Broilers	combination	Farm	Farm	Isolate	Contingency Table	0.5	21.5	0.5	12.5
Heuer, 2001	28	Across Studies, Same Antimicrobial Class	Broilers	combination	Farm	Farm	Isolate	Contingency Table	1.5	28.5	0.5	12.5
Luangtongkum, 2006	29	Across Studies, Same Antimicrobial Class	Carcass	Combination	Farm	Farm	Isolate	Contingency Table	15.5	150.5	0.5	167.5
Meta-analysis	30	Across Studies, Same Antimicrobial Class	Broilers	spp.	Farm	NA	NA	Odds Ratio	NA	NA	NA	NA
Adiguzel, 2018	31	Across Studies, Same Antimicrobial Class	Carcass	combination	Farm	Farm	Isolate	Contingency Table	63	3	51	28
Luangtongkum, 2006	32	Across Studies, Same Antimicrobial Class	Carcass	Combination	Farm	Farm	Isolate	Contingency Table	0.5	165.5	77.5	90.5

Paper Ref	ID	Meta-Analysis Type	Host	*Campylobacter* species	Allocation Stage	Observed Stage	Unit of Sampling	Result Format	A	B	C	D
Meta-analysis	33	Across Studies, Same Antimicrobial Class	Carcass	spp.	Farm	NA	NA	Odds Ratio	NA	NA	NA	NA
Adiguzel, 2018	34	Across Studies, Same Antimicrobial Class	Carcass	combination	Farm	Farm	Isolate	Contingency Table	64.5	2.5	0.5	79.5
Bester, 2012	35	Across Studies, Same Antimicrobial Class	Broilers	Other	Farm	Farm	Isolate	Prevalence Table	66.5	0.5	62.5	1.5
Heuer, 2001	36	Across Studies, Same Antimicrobial Class	Broilers	combination	Farm	Farm	Isolate	Contingency Table	1.5	20.5	0.5	12.5
Heuer, 2001	37	Across Studies, Same Antimicrobial Class	Broilers	combination	Farm	Farm	Isolate	Contingency Table	0.5	29.5	0.5	12.5
Luangtongkum, 2006	38	Across Studies, Same Antimicrobial Class	Carcass	Combination	Farm	Farm	Isolate	Contingency Table	99	66	141	26
Meta-analysis	39	Across Studies, Same Antimicrobial Class	Carcass	spp.	Farm	NA	NA	Odds Ratio	NA	NA	NA	NA
Humphrey, 2005	40	Within Study, Same Antimicrobial Class	Broilers	Combination	Farm	Farm	Sample	Contingency Table	11	2	2	12
Humphrey, 2005	41	Within Study, Same Antimicrobial Class	Broilers	Combination	Farm	Farm	Sample	Contingency Table	10	2	1	13
Humphrey, 2005	42	Within Study, Same Antimicrobial Class	Broilers	Combination	Farm	Farm	Sample	Contingency Table	10.5	4.5	0.5	13.5
Humphrey, 2005	43	Within Study, Same Antimicrobial Class	Broilers	Combination	Farm	Farm	Sample	Contingency Table	13.5	0.5	4.5	10.5
Humphrey, 2005	44	Within Study, Same Antimicrobial Class	Broilers	Combination	Farm	Farm	Sample	Contingency Table	8	6	4	7
Meta-analysis	45	Within Study, Same Antimicrobial Class	Broilers	spp.	Farm	NA	NA	Odds Ratio	NA	NA	NA	NA
Takahashi, 2005	46	Across Studies, Same Antimicrobial Class	Broilers	unspeciated	Farm	Farm	Sample	Prevalence Table	10.5	0.5	0.5	10.5
Takahashi, 2005	47	Across Studies, Same Antimicrobial Class	Broilers	unspeciated	Farm	Farm	Sample	Prevalence Table	10.5	0.5	0.5	10.5
Takahashi, 2005	48	Across Studies, Same Antimicrobial Class	Broilers	unspeciated	Farm	Farm	Sample	Prevalence Table	0.5	10.5	0.5	10.5
Takahashi, 2005	49	Across Studies, Same Antimicrobial Class	Broilers	unspeciated	Farm	Farm	Sample	Prevalence Table	0.5	10.5	0.5	10.5
Meta-analysis	50	Within Study, Same Antimicrobial Class	Broilers	jejuni	Farm	NA	NA	Odds Ratio	NA	NA	NA	NA
Takahashi, 2005	51	Within Study, Same Antimicrobial Class	Broilers	jejuni	Farm	Farm	Sample	Prevalence Table	10.5	0.5	0.5	10.5
Takahashi, 2005	52	Within Study, Same Antimicrobial Class	Broilers	jejuni	Farm	Farm	Sample	Prevalence Table	10.5	0.5	0.5	10.5
Takahashi, 2005	53	Within Study, Same Antimicrobial Class	Broilers	jejuni	Farm	Farm	Sample	Prevalence Table	0.5	10.5	0.5	10.5
Takahashi, 2005	54	Within Study, Same Antimicrobial Class	Broilers	jejuni	Farm	Farm	Sample	Prevalence Table	0.5	10.5	0.5	10.5
Jacobs-Reitsma, 1994	55	Within Study, Same Antimicrobial Class	Chicks	jejuni	Farm	Farm	Isolate	Contingency Table	0.5	8.5	0.5	3.5
Jacobs-Reitsma, 1994	56	Within Study, Same Antimicrobial Class	Chicks	jejuni	Farm	Farm	Isolate	Contingency Table	0.5	8.5	0.5	3.5
Jacobs-Reitsma, 1994	57	Within Study, Same Antimicrobial Class	Chicks	jejuni	Farm	Farm	Isolate	Contingency Table	0.5	8.5	0.5	3.5
Jacobs-Reitsma, 1994	58	Within Study, Same Antimicrobial Class	Chicks	jejuni	Farm	Farm	Isolate	Contingency Table	0.5	8.5	0.5	3.5
Meta-analysis	59	Within Study, Same Antimicrobial Class	Chicks	jejuni	Farm	NA	NA	Odds Ratio	NA	NA	NA	NA
Jacobs-Reitsma, 1994	60	Within Study, Same Antimicrobial Class	Chicks	jejuni	Farm	Farm	Isolate	Contingency Table	8.5	0.5	0.5	3.5
Jacobs-Reitsma, 1994	61	Within Study, Same Antimicrobial Class	Chicks	jejuni	Farm	Farm	Isolate	Contingency Table	8.5	0.5	0.5	3.5
Jacobs-Reitsma, 1994	62	Within Study, Same Antimicrobial Class	Chicks	jejuni	Farm	Farm	Isolate	Contingency Table	8.5	0.5	0.5	3.5
Jacobs-Reitsma, 1994	63	Within Study, Same Antimicrobial Class	Chicks	jejuni	Farm	Farm	Isolate	Contingency Table	8.5	0.5	0.5	3.5
Jacobs-Reitsma, 1994	64	Within Study, Same Antimicrobial Class	Chicks	jejuni	Farm	Farm	Isolate	Contingency Table	0.5	3.5	0.5	3.5

Paper Ref	ID	Meta-Analysis Type	Host	*Campylobacter* species	Allocation Stage	Observed Stage	Unit of Sampling	Result Format	A	B	C	D
Jacobs-Reitsma, 1994	65	Within Study, Same Antimicrobial Class	Chicks	jejuni	Farm	Farm	Isolate	Contingency Table	0.5	3.5	0.5	3.5
Meta-analysis	66	Within Study, Same Antimicrobial Class	Chicks	jejuni	Farm	NA	NA	Odds Ratio	NA	NA	NA	NA
Jacobs-Reitsma, 1994	67	Within Study, Same Antimicrobial Class	Chicks	jejuni	Farm	Farm	Isolate	Contingency Table	0.5	8.5	0.5	3.5
Jacobs-Reitsma, 1994	68	Within Study, Same Antimicrobial Class	Chicks	jejuni	Farm	Farm	Isolate	Contingency Table	0.5	8.5	0.5	3.5
Meta-analysis	69	Within Study, Same Antimicrobial Class	Chicks	jejuni	Farm	NA	NA	Odds Ratio	NA	NA	NA	NA
Jacobs-Reitsma, 1994	70	Across Studies, Same Antimicrobial Class	Chicks	jejuni	Farm	Farm	Isolate	Contingency Table	8.5	0.5	0.5	3.5
Jacobs-Reitsma, 1994	71	Across Studies, Same Antimicrobial Class	Chicks	jejuni	Farm	Farm	Isolate	Contingency Table	8.5	0.5	0.5	3.5
Jacobs-Reitsma, 1994	72	Across Studies, Same Antimicrobial Class	Chicks	jejuni	Farm	Farm	Isolate	Contingency Table	0.5	3.5	0.5	3.5
McDermott, 2002	73	Across Studies, Same Antimicrobial Class	Broilers	jejuni	Farm	Farm	Isolate	Prevalence Table	49.5	1.5	0.5	50.5
Meta-analysis	74	Across Studies, Same Antimicrobial Class	Chicks	jejuni	Farm	NA	NA	Odds Ratio	NA	NA	NA	NA
Meta-analysis	75	Within Study, Same Antimicrobial Class	Broilers	Combination	Abattoir	NA	NA	Odds Ratio	NA	NA	NA	NA
Sanchez, 2002	76	Within Study, Same Antimicrobial Class	Broilers	Combination	Abattoir	Abattoir	Carcass	Prevalence Table	43	30	11	48
Sanchez, 2002	77	Within Study, Same Antimicrobial Class	Broilers	Combination	Abattoir	Abattoir	Carcass	Prevalence Table	6.5	67.5	0.5	59.5
Sanchez, 2002	78	Within Study, Same Antimicrobial Class	Broilers	Combination	Abattoir	Abattoir	Carcass	Prevalence Table	30	43	5	54
Sanchez, 2002	79	Within Study, Same Antimicrobial Class	Broilers	Combination	Abattoir	Abattoir	Carcass	Prevalence Table	30	43	11	48
Adiguzel, 2018	80	NA	Carcass	combination	Farm	Farm	Isolate	Contingency Table	0.5	66.5	0.5	79.5
Asai, 2007	81	NA	Broilers	jejuni	Farm	Farm	Farm	Contingency Table	2.5	0.5	18.5	60.5
Asai, 2007	82	NA	Broilers	jejuni	Farm	Farm	Farm	Contingency Table	3	4	33	40
Asai, 2007	83	NA	Broilers	coli	Farm	Farm	Farm	Contingency Table	0.5	0.5	5.5	8.5
Asai, 2007	84	NA	Broilers	coli	Farm	Farm	Farm	Contingency Table	2.5	0.5	5.5	6.5
Avrain, 2003	85	NA	Carcass	jejuni	Farm	Farm	Flock	Contingency Table	55	30	58	63
Avrain, 2003	86	NA	Carcass	jejuni	Farm	Farm	Flock	Contingency Table	6	10	7	50
Avrain, 2003	87	NA	Carcass	coli	Farm	Farm	Flock	Contingency Table	16	10	6	15
Hoogenboom, 2008	88	NA	Broilers	Not Specified	Farm	Farm	Sample	Prevalence Table	17	15	23	34
Hoogenboom, 2008	89	NA	Broilers	Not Specified	Farm	Farm	Sample	Prevalence Table	14	18	26	31
Hoogenboom, 2008	90	NA	Broilers	Not Specified	Farm	Farm	Sample	Prevalence Table	0.5	32.5	0.5	57.5
Hoogenboom, 2008	91	NA	Broilers	Not Specified	Farm	Farm	Sample	Prevalence Table	17	15	23	34
Ladely, 2007	92	NA	Broilers	coli	Farm	Farm	Animal	Contingency Table	10.5	0.5	2.5	1.5
Ladely, 2007	93	NA	Broilers	jejuni	Farm	Farm	Animal	Contingency Table	11	4	2	10
Ladely, 2007	94	NA	Broilers	combination	Farm	Farm	Animal	Contingency Table	21.5	0.5	4.5	11.5
Sanchez, 2002	95	NA	Broilers	Combination	Abattoir	Abattoir	Carcass	Prevalence Table	36	37	5	54

Paper Ref	ID	Meta-Analysis Type	Host	*Campylobacter* species	Allocation Stage	Observed Stage	Unit of Sampling	Result Format	A	B	C	D
Sanchez, 2002	96	NA	Broilers	Combination	Abattoir	Abattoir	Carcass	Prevalence Table	30	43	11	48
Sanchez, 2002	97	NA	Broilers	Combination	Abattoir	Abattoir	Carcass	Prevalence Table	12	61	54	5
Soonthornchaikul, 2006	98	NA	Carcass	Not Specified	Retail	Retail	Carcass	Prevalence Table	30.5	0.5	30.5	0.5
Soonthornchaikul, 2006	99	NA	Carcass	Not Specified	Retail	Retail	Carcass	Prevalence Table	30.5	0.5	30.5	0.5
Soonthornchaikul, 2006	100	NA	Carcass	Not Specified	Retail	Retail	Carcass	Prevalence Table	8	22	3	27
Stapleton, 2010	101	NA	Broilers	jejuni	Farm	Farm	Isolate	Contingency Table	68	28	147	69
Stapleton, 2010	102	NA	Broilers	jejuni	Farm	Farm	Isolate	Contingency Table	222	70	147	69
Stapleton, 2010	103	NA	Broilers	jejuni	Farm	Farm	Isolate	Prevalence Table	145	1	71	139
Stapleton, 2010	104	NA	Broilers	jejuni	Farm	Farm	Isolate	Prevalence Table	158	159	71	139

Paper Ref	ID	P	R	Q	S	Total Exposed	Total Referent
Heuer, 2001	1	NA	NA	NA	NA	2	2
Heuer, 2001	2	NA	NA	NA	NA	5	2
Meta-analysis	3	NA	NA	NA	NA	NA	NA
Heuer, 2001	4	NA	NA	NA	NA	2	2
Heuer, 2001	5	NA	NA	NA	NA	5	2
Meta-analysis	6	NA	NA	NA	NA	NA	NA
Heuer, 2001	7	NA	NA	NA	NA	2	2
Heuer, 2001	8	NA	NA	NA	NA	5	2
Meta-analysis	9	NA	NA	NA	NA	NA	NA
Heuer, 2001	10	NA	NA	NA	NA	19	10
Heuer, 2001	11	NA	NA	NA	NA	24	10
Meta-analysis	12	NA	NA	NA	NA	NA	NA
Heuer, 2001	13	NA	NA	NA	NA	19	10
Heuer, 2001	14	NA	NA	NA	NA	24	10
Meta-analysis	15	NA	NA	NA	NA	NA	NA
Heuer, 2001	16	NA	NA	NA	NA	19	10
Heuer, 2001	17	NA	NA	NA	NA	24	10
Meta-analysis	18	NA	NA	NA	NA	NA	NA
Adiguzel, 2018	19	NA	NA	NA	NA	66	79
Bester, 2012	20	95.4	NA	15.9	NA	66	63
Heuer, 2001	21	NA	NA	NA	NA	21	12
Heuer, 2001	22	NA	NA	NA	NA	29	12
Luangtongkum, 2006	23	NA	NA	NA	NA	165	167
Luangtongkum, 2006	24	NA	NA	NA	NA	165	167
Meta-analysis	25	NA	NA	NA	NA	NA	NA
Bester, 2012	26	87.9	NA	47.6	NA	66	63
Heuer, 2001	27	NA	NA	NA	NA	21	12
Heuer, 2001	28	NA	NA	NA	NA	29	12
Luangtongkum, 2006	29	NA	NA	NA	NA	165	167
Meta-analysis	30	NA	NA	NA	NA	NA	NA
Adiguzel, 2018	31	NA	NA	NA	NA	66	79
Luangtongkum, 2006	32	NA	NA	NA	NA	165	167
Meta-analysis	33	NA	NA	NA	NA	NA	NA
Adiguzel, 2018	34	NA	NA	NA	NA	66	79
Bester, 2012	35	100	NA	98.9	NA	66	63
Heuer, 2001	36	NA	NA	NA	NA	21	12
Heuer, 2001	37	NA	NA	NA	NA	29	12
Luangtongkum, 2006	38	NA	NA	NA	NA	165	167
Meta-analysis	39	NA	NA	NA	NA	NA	NA
Humphrey, 2005	40	NA	NA	NA	NA	13	14
Humphrey, 2005	41	NA	NA	NA	NA	12	14
Humphrey, 2005	42	NA	NA	NA	NA	14	13
Humphrey, 2005	43	NA	NA	NA	NA	13	14
Humphrey, 2005	44	NA	NA	NA	NA	14	11
Meta-analysis	45	NA	NA	NA	NA	NA	NA

Paper Ref	ID	P	R	Q	S	Total Exposed	Total Referent
Takahashi, 2005	46	100	NA	0	NA	10	10
Takahashi, 2005	47	100	NA	0	NA	10	10
Takahashi, 2005	48	0	NA	0	NA	10	10
Takahashi, 2005	49	0	NA	0	NA	10	10
Meta-analysis	50	NA	NA	NA	NA	NA	NA
Takahashi, 2005	51	100	NA	0	NA	10	10
Takahashi, 2005	52	100	NA	0	NA	10	10
Takahashi, 2005	53	0	NA	0	NA	10	10
Takahashi, 2005	54	0	NA	0	NA	10	10
Jacobs-Reitsma, 1994	55	NA	NA	NA	NA	8	3
Jacobs-Reitsma, 1994	56	NA	NA	NA	NA	8	3
Jacobs-Reitsma, 1994	57	NA	NA	NA	NA	8	3
Jacobs-Reitsma, 1994	58	NA	NA	NA	NA	8	3
Meta-analysis	59	NA	NA	NA	NA	NA	NA
Jacobs-Reitsma, 1994	60	NA	NA	NA	NA	8	3
Jacobs-Reitsma, 1994	61	NA	NA	NA	NA	8	3
Jacobs-Reitsma, 1994	62	NA	NA	NA	NA	8	3
Jacobs-Reitsma, 1994	63	NA	NA	NA	NA	8	3
Jacobs-Reitsma, 1994	64	NA	NA	NA	NA	3	3
Jacobs-Reitsma, 1994	65	NA	NA	NA	NA	3	3
Meta-analysis	66	NA	NA	NA	NA	NA	NA
Jacobs-Reitsma, 1994	67	NA	NA	NA	NA	8	3
Jacobs-Reitsma, 1994	68	NA	NA	NA	NA	8	3
Meta-analysis	69	NA	NA	NA	NA	NA	NA
Jacobs-Reitsma, 1994	70	NA	NA	NA	NA	8	3
Jacobs-Reitsma, 1994	71	NA	NA	NA	NA	8	3
Jacobs-Reitsma, 1994	72	NA	NA	NA	NA	3	3
McDermott, 2002	73	98	NA	0	NA	50	50
Meta-analysis	74	NA	NA	NA	NA	NA	NA
Meta-analysis	75	NA	NA	NA	NA	NA	NA
Sanchez, 2002	76	58.3	NA	18.2	NA	73	59
Sanchez, 2002	77	8.3	NA	0	NA	73	59
Sanchez, 2002	78	41.7	NA	9.1	NA	73	59
Sanchez, 2002	79	41.7	NA	18.2	NA	73	59
Adiguzel, 2018	80	NA	NA	NA	NA	66	79
Asai, 2007	81	NA	NA	NA	NA	2	78
Asai, 2007	82	NA	NA	NA	NA	7	73
Asai, 2007	83	NA	NA	NA	NA	0	13
Asai, 2007	84	NA	NA	NA	NA	2	11
Avrain, 2003	85	NA	NA	NA	NA	85	121
Avrain, 2003	86	NA	NA	NA	NA	16	57
Avrain, 2003	87	NA	NA	NA	NA	26	21
Hoogenboom, 2008	88	53.3	NA	40.56	NA	32	57
Hoogenboom, 2008	89	43.7	NA	45.7	NA	32	57

Paper Ref	ID	P	R	Q	S	Total Exposed	Total Referent
Hoogenboom, 2008	90	0	NA	0	NA	32	57
Hoogenboom, 2008	91	53.3	NA	40.54	NA	32	57
Ladely, 2007	92	NA	NA	NA	NA	10	3
Ladely, 2007	93	NA	NA	NA	NA	15	12
Ladely, 2007	94	NA	NA	NA	NA	21	15
Sanchez, 2002	95	50	NA	9.1	NA	73	59
Sanchez, 2002	96	41.7	NA	18.2	NA	73	59
Sanchez, 2002	97	16.7	NA	90.9	NA	73	59
Soonthornchaikul, 2006	98	100	NA	100	NA	30	30
Soonthornchaikul, 2006	99	100	NA	100	NA	30	30
Soonthornchaikul, 2006	100	26.7	NA	8.7	NA	30	30
Stapleton, 2010	101	NA	NA	NA	NA	96	216
Stapleton, 2010	102	NA	NA	NA	NA	292	216
Stapleton, 2010	103	99	NA	34	NA	146	210
Stapleton, 2010	104	50	NA	34	NA	317	210

APPENDIX 3.6

FoodNet Canada Packaging Type Data

[In the following pages]

Data Request: UofAlberta	
December 2021	
FNC Component:	Retail, proportion of broiler chicken samples at retail that are packaged at counter vs pre-packaged
Results and/or variables requested:	Overall proportion and counts of broiler chicken samples at retail that are packaged at counter and proportion and counts of broiler chicken samples at retail that are pre-packaged, separated out by year
Type of data:	Agrgregate
Years requested:	2015- present
Notes:	2021 data has yet to be validated, for this reason it has been omitted from analysis 2020 data had significant disruptions in sample collection due to the COVID-19 pandemic

Package type in Retail Chicken, 2015-2020

Package Type	2015	2016	2017	2018	2019	2020	Total
Packaged at Counter	n=24	n=46	n=51	n=60	n=85	n=23	289
	5.99%	11.62%	13.08%	15.38%	19.32%	14.29%	
Pre-packaged	n=377	n=350	n=339	n=330	n=355	n=138	1889
	94.01%	88.38%	86.92%	84.62%	80.68%	85.71%	
Total	401	396	390	390	440	161	2178