A scoping review of factors associated with antimicrobial-resistant Campylobacter species infections in humans

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Summary

Human infection with antimicrobial-resistant *Campylobacter* species is an important public health concern due to potentially increased severity of illness and risk of death. Our objective was to synthesize knowledge of factors associated with human infection with antimicrobial-resistant strains of *Campylobacter*. This scoping review followed systematic methods, including a protocol developed *a priori*. Comprehensive literature searches were developed in consultation with a research librarian and performed in five primary and three grey literature databases. Criteria for inclusion were analytical and English-language publications investigating human infections with an antimicrobial-resistant (macrolides, tetracyclines, fluoroquinolones, and/or quinolones) *Campylobacter* that reported factors potentially linked with the infection. Primary and secondary screening were completed by two independent reviewers using Distiller SR®. The search identified 8,527 unique articles and included 27 articles in the review. Factors were broadly categorized into animal contact, prior antimicrobial use, participant characteristics, food consumption and handling, travel, underlying health conditions, and water consumption/exposure. Important factors linked to increased risk of infection with a fluoroquinolone-resistant strain included foreign travel and prior antimicrobial use. Identifying consistent risk factors was challenging due to the heterogeneity of results, inconsistent analysis, and the lack of data in low- and middle-income countries, highlighting the need for future research.
Introduction

*Campylobacter* species is one of the leading causes of acute diarrheic illness, accounting for 16% of foodborne illness globally [1] and 8.42% of foodborne illness in Canada [2]. Infections are characterized by acute, watery diarrhoea progressing to bloody diarrhoea and often accompanied by abdominal pain, but vomiting is uncommon [3]. *Campylobacter* infection has an incubation period of 2-4 days and most people recover within 2-5 days [4]. An uncomplicated infection typically only requires supportive care to avoid dehydration [4]; however, some cases develop bacteremia [5]. Although uncommon, complications related to *Campylobacter* infection include but are not limited to: reactive arthritis, irritable bowel syndrome, Guillain-Barré Syndrome (GBS), and Miller Fisher Syndrome, a variant of GBS, which are autoimmune disorders characterized by nerve damage, muscle weakness and sometimes paralysis [5, 6].

Fluoroquinolone and macrolide antimicrobials can be used in the treatment of complicated *Campylobacter* infections to reduce duration of illness [7]. There is evidence that inappropriate antimicrobial prescribing practices occur in Canada for *Campylobacter* infections, such as: prescribing antimicrobials after symptoms have resolved, before the culture results have confirmed the diagnosis of *Campylobacter*, or treatment before the collection of a sample [8]. Furthermore, antimicrobials not suggested by prescribing guidelines have also been prescribed [9]. Human infection with strains resistant to macrolides, fluoroquinolones/quinolones and other antimicrobial classes including tetracyclines occur [10], and these infections 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 [11-13].

There is a large amount of research on factors associated with human *Campylobacter* infections, including undercooked meat, especially chicken, contaminated unpasteurized milk,
animal contact, and contaminated water [4]. However, despite this wealth of research, searches on January 21, 2020, in Ovid Medline®, Cochrane Library, Joanna Briggs Institute Systematic Review Registry, and Google Scholar did not identify any scoping or systematic reviews on factors associated with infection with antimicrobial-resistant Campylobacter. The objective of this scoping review was to synthesize the published literature on factors associated with human infection with antimicrobial-resistant strains of Campylobacter species, with focus on resistance to macrolides, tetracyclines, fluoroquinolones and/or quinolones.

Methods

Protocol, search, and information sources

The review followed systematic search methods outlined in the Joanna Briggs Institute (JBI) Reviewer’s Manual [14] and is reported according to the PRISMA Scoping Review reporting guidelines [15]. The protocol was registered with the JBI Systematic Review Register on February 5, 2020, and is available in the Supplementary Material (S1). The PRISMA-Scoping Review checklist is provided in Supplementary Table S1.

A comprehensive search strategy was developed in consultation with a librarian to identify articles that studied human infection with antimicrobial-resistant Campylobacter. An example search string for MEDLINE® in Ovid® is shown in Supplementary Table S2. The complete search strings (S1) were used to search MEDLINE®, AGRICOLA™ in ProQuest®, Centre for Agriculture and Bioscience abstracts in Web of Science, EMBASE® in Ovid, and Scopus®. Grey literature sources included: the World Health Organization’s Global Index Medicus, the Bielefeld Academic Search Engine, and the first 250 results from Google Scholar when sorted by relevance. The search was completed on February 5, 2020, and was updated on
May 7, 2021. Articles were de-duplicated in three stages in Mendeley (Version 1.19.8, Elsevier, Amsterdam, Netherlands), EndNote (Version X9.2, Clarivate Analytics, London, United Kingdom), and DistillerSR (Version 2.35, Evidence Partners, Ottawa, ON, Canada).

**Eligibility criteria**

To be included, articles including theses and dissertations had to be an analytic study that used a comparison group and reported on factors potentially associated with human infection with a strain of *Campylobacter* resistant to an antimicrobial of interest: macrolides, tetracyclines, and fluoroquinolones/quinolones (collectively referred to as fluoroquinolones hereafter). Resistance had to be determined by recognized laboratory antimicrobial susceptibility testing methods such as disk diffusion or broth micro-dilution. Review articles, commentaries, opinion pieces, editorials, newspaper articles, books, book chapters, and conference proceedings were excluded. No limits were applied to language, geographical location, *Campylobacter* species, or date of publication. Non-English articles identified during primary screening were excluded. Included studies had to report humans *Campylobacter* infection confirmed by recognized laboratory methods. Studies on non-human research, infections other than *Campylobacter*, colonization instead of infection, or that failed to confirm a *Campylobacter* infection by recognized laboratory methods were excluded.

Factors associated with human infection with a resistant strain of *Campylobacter* were defined as observations that were measured and quantified, with potential for identifying a reported statistical relationship to antimicrobial resistance (AMR) [16], which included but were not limited to age, recent travel, or pre-existing medical conditions. The comparator group had to be appropriate for the study design. For example, the comparator group for case-control studies...
were infections with strains of *Campylobacter* that were susceptible to the antimicrobials of interest. Inherently, the comparator group had to be *Campylobacter* isolates from human infections that were susceptible to the antimicrobials of interest, to compare to the resistant isolates from human infections.

Articles were screened for eligibility via a two-stage screening process by two independent reviewers. Article titles, abstracts, and key words were screened in the first stage and articles proceeded to secondary screening if both reviewers determined all eligibility criteria was met or unclear (S1). Secondary full-text screening by both reviewers included articles that answered yes to all eligibility criteria. The reasons for exclusion were documented. Reviewers resolved conflicts through discussion.

**Data collection and synthesis**

Data regarding authorship, publication date, location of study, study type (defined by the authors or assigned by the reviewers), AMR outcome(s), *Campylobacter* species, site of infection, factor description and descriptive data, results of measures of association (if considered), and type of analysis (univariable versus multivariable where reported) were extracted by one reviewer in Distiller SR® and analyzed in Excel® (Microsoft, Redmond, WA) and using the R Metaphor package (v4.1.1, R Core Team, 2021). Tables and figures present key findings in the results, while supplementary materials provide comprehensive results from the study. Factors were combined into themed categories for comparison. For relative associations, an odds ratio with a value of less than one is generally interpreted as a protective factor while a value greater than one was interpreted as a risk factor, meaning that either were associated with a decreased or increased risk of infection with a resistant strain of *Campylobacter*, respectively.
Results

Selection of information sources

Our search identified 8,527 unique articles. Primary and secondary screening excluded 8,089 and 411 articles, respectively, including 12 where we could not locate a full-text document after additional inquiry through library requests (Figure 1). The review included 27 articles that met all inclusion criteria.

Characteristics of information sources

Characteristics of included articles (n=27) are included in Table 1. Complete extracted data for all studies are included in Supplementary Table S3. All articles were published between 1998-2018 except for one in 1988. The most common countries included: the United States (n=6), Denmark (n=4), Canada (n=3), and the United Kingdom (n=3). Study designs included cross-sectional (n=16), case-control (n=4), case-case-control (n=1), and various cohort designs (n=6). The most common reported age range of participants was 20-50 years, but variations in reporting details made summarizing age characteristics difficult. Fourteen studies reported gender or sex of participants, but rarely included it in analysis, while the rest did not report (n=9) or did not include females in their study (n=4). Most articles studied gastrointestinal infections (n=19) and the most common species included was Campylobacter jejuni (n=22). Six studies reported results for multivariable analyses, while the remaining 21 only reported results from univariable analyses if at all. Often, studies reported resistance to different antimicrobials. The most reported factor results were for resistance to fluoroquinolones (n=20) and quinolones (n=9) while resistance to macrolides (n=13) and tetracyclines (n=7) were also considered.
Information about factors

Reported factors related to resistant *Campylobacter* infections are summarized in Supplementary Table S4 and were combined into seven themes: animal contact (Figure 2), prior antimicrobial use (Figure 3), food and food preparation (Figures 4A and B), travel (Figure 5), underlying health conditions (Supplementary Table S5), water exposure (Figures 6A and B), and participant characteristics (Supplementary Table S5). Articles reporting factors regarding travel (n=17) and participant characteristics (n=14) were most common. Most of the studies were conducted in a small number of high-income, westernized countries. Studies reported data for unspecified *Campylobacter* species as well as *C. jejuni*, *C. coli*, *C. fetus*, and *C. lari*.

Synthesis of results

Animal contact

Five articles reported animal contact as a factor for infection with fluoroquinolone-resistant strains of *Campylobacter* (Figure 2). Most factors, including unspecified pets, pet rodents, dogs, birds, and other domestic or animal contact, were associated with a decreased risk of infection with resistant *Campylobacter* [12, 17-19]. Zoo animal contact was the only animal factor that was significantly associated with an increased risk [17].

Prior antimicrobial use

Seven articles reported prior antimicrobial use as a factor [12, 17, 20-24], but only five reported results of analysis. All studies with speciated isolates found that prior antimicrobial use was associated with an increased risk of infection with fluoroquinolone-resistant *Campylobacter*, but not all were statistically significant (Figure 3). The study with non-speciated isolates found
prior antimicrobial use was associated with lower risk, but it was not significant. The definition of prior antimicrobial use varied between studies, ranging from possession of non-prescribed antibiotics [21] to use of an antibiotic before specimen collection [12, 24]. In addition, the definition of the interval for prior antimicrobial use was a month (four weeks) [12, 17, 20, 24, 25], but when specified, the start point of this interval also varied from a month prior to onset of illness [20, 24], onset of symptoms [12], infection [25], or stool sample collection [21].

**Food and food preparation**

Four articles reported many different factors related to food consumption and food handling or associated behaviours, all with fluoroquinolone resistance outcomes (Figures 4A and B) [12, 17-19]. There were opposing results of varying statistical significance for factors such as consumption of chicken, red meat, and other miscellaneous meats, as well as for handling of raw meat and raw chicken at home [12, 17-19] without any discernable pattern. When considering multivariable results, one study reported that those eating chicken had decreased risk, but increased risk when eating poultry other than chicken or turkey [12]. Another reported increased risk when eating chicken or pre-cooked cold meats [18]. Interestingly, two studies found that factors linked to handling [12] or storing of raw chicken [17] were significantly associated with a reduced risk for infection with a fluoroquinolone-resistant strain, while the latter paper found no association with handling raw chicken, all from univariable analyses.

**Travel**

Seventeen studies reported travel-related factors related to an infection with resistant *Campylobacter* (Figure 5) [11, 12, 17-19, 21, 24-34], and all found foreign travel, regardless of
definition and destination country, to be significantly associated with an increased risk of
infection with a fluoroquinolone-resistant strain. Of the articles that reported analysis, domestic
study populations were limited to the United Kingdom [18], Wales [17], Denmark [12], Canada
[21], and the United States [19, 21, 24, 30, 31]. Travel destinations included Africa, Asia,
Central and South America, and Europe, but some articles conducted sub-analyses on
destinations within travel-only cases, which made interpretation challenging [18, 24, 29]. One
study considered food and water exposure during travel but did not evaluate travel as a possible
interaction [17]. Another study compared the rate of fluoroquinolone-resistant C. jejuni
infections in Finnish patients that travelled abroad; specifically comparing rates of cases from
various travel destinations to those travelling to Thailand [29]. They found that cases in Finnish
residents travelling to Spain (including the Canary Islands) and Portugal had lower case rates of
fluoroquinolone-resistant infections (rate ratios of 0.11 [95% CI 0.05-0.24] and 0.11 [0.07-0.16],
respectively), while those traveling to China and India did not differ significantly from Thailand.

Water

Four articles explored factors related to water exposure, with a focus on water
consumption and swimming [12, 17, 18, 24]. There was a large variety in definition of water
consumption-related factors and their association with increased or decreased risk of infection
with fluoroquinolone-resistant strains (Figure 6A). Untreated water was associated with
increased risk [24], while public, tap, or private domestic water were associated with decreased
risk [12, 17, 18]. Several bottled water (domestic or travel-sourced) factors were associated with
increased risk [17, 18]. Generally, swimming was reported to increase the risk of infection with a
resistant strain (Figure 6B).
Underlying conditions

Five studies explored factors related to underlying health conditions (Supplementary Table S5), but three did not analyze the data for association [17, 23, 30, 35, 36]. Of the two that did [17, 30], the only statistically significant factor was patients with diabetes (OR 0.30, 95% CI 0.10-1.00) [17]. Antacid use within the past month, indicating other potential conditions, was not significant (OR 1.50, 95% CI 0.90-2.40) [30]. Three studies investigated risk associated with HIV infection but did not complete analysis on their data [23, 35, 36].

Patient characteristics

Thirteen articles explored multiple factors related to participant characteristics such as season of infection, level of education, household income, gender, sex, and age (see Supplementary Table S5) [17-19, 21, 28-31, 37-41]. Factor definitions and results were highly variable and only four articles conducted multivariable analyses on their data [17-19, 21].

Discussion

Summary of evidence

This scoping review identified 27 studies with factors related to human infection with an antimicrobial-resistant strain of *Campylobacter* and provides insight into the available literature and risks associated with these infections. Many reported specific gastrointestinal infections with *C. jejuni*, but there was variability in the site of infection (sample source and *Campylobacter* species), the AMR outcome, and subsequent factor analyses. This review identified key factors associated with infection with resistant strains, such as travel, prior antimicrobial use, animal exposure, and food and water-related factors, but highlighted the vast heterogeneity of available
data and associations with increased or decreased risk of infection with a resistant strain, as well as the gaps that could benefit from further research. Only a small number of studies reported multivariable analysis, and those that did were almost exclusively for fluoroquinolone resistance outcomes. All studies were conducted on cases from a small number of wealthy, westernized countries.

**Risk factors**

This review identified several important risk factors associated with human infection with resistant *Campylobacter*. The most consistent was foreign travel, with departure from home countries always being significantly associated with infection with a fluoroquinolone-resistant strain [12, 17, 19, 24, 25, 30, 31, 33, 34]. Care needs to be taken when interpreting these results as only departures from a few wealthy, westernized countries were studied, with highly variable definition of destinations. Travel is a complex variable that, in this context, is largely a proxy for several different, often unmeasured, factors in the destination country, such as water quality, food/food handling practices and microbial contamination, and potential exposure to different strains of pathogens [42]. Genomics and molecular epidemiology should be employed to better understand the epidemiology of antimicrobial-resistant *Campylobacter* infection in future observational risk factor studies.

Antimicrobial use prior to infection was another important reported factor for infection with resistant *Campylobacter*. While prior antimicrobial use is recognized to select for AMR, especially in *Campylobacter* [43, 44], only seven of the included studies reported this factor [12, 17, 20-24]. It is possible that many studies did not have access to these data linked to the human cases, which can be difficult to collect/obtain. It is important to note that in these studies, it
represents a risk factor for infection with resistant *Campylobacter* compared to susceptible infection, but these observational studies cannot determine whether prior antimicrobial use specifically selected for a resistant strain in the human host. In addition to the inconsistent definitions of prior antimicrobial use, no studies reported drug dosing or duration, which would be important for future quantitative dose-response modeling. Prior antimicrobial use has been identified as a risk factor for other antimicrobial-resistant, foodborne bacterial infections, such as *Salmonella* Heidelberg [45]. Prior antimicrobial use may be due to inappropriate prescribing or over-the-counter drug access, which may represent less than optimal antimicrobial stewardship [44]. Only one included study reported a factor in this realm, possession of non-prescribed antibiotics [21]. 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* and did not analyse their data beyond providing counts [23, 35, 39].

Animal contact, including contact with seemingly healthy pets, has been implicated as a risk factor for AMR in humans [46-48], as well as general human infection with *Campylobacter*. Resistant *Campylobacter* has been isolated from cats and dogs, and pet store puppies have been implicated in a large extensively drug-resistant human outbreak of *C. jejuni* [49, 50]. Conversely, the included studies found that in most cases, animal contact was associated with a reduced risk of infection with resistant compared to susceptible *Campylobacter* [12, 17-19, 24], with the one exception being zoo animal contact [17]. It may be that in these studies, the infecting strains from different animal sources have varying antimicrobial susceptibilities, but these observational study designs were not able to distinguish this, pointing to the need for genomics and molecular epidemiology to better understand these identified associations.
Contaminated foods, especially chicken meat, are known risk factors for infection with *Campylobacter* [4, 51], but only four studies included food-related factors in their analysis [12, 17-19]. There is evidence of AMR spreading to humans through the food chain, specifically broiler chickens in the case of *Campylobacter*, where antimicrobial use on farm may initially select for AMR [16, 52]. However, the results of food-related factors, including chicken, from included studies are mixed and variable. There are several potential reasons for this, including different study populations and potential confounding, intervening, or unmeasured factors, many of which were not considered in studies that did not conduct multivariable analyses. Many studies were cross-sectional, making causal inference for these relationships challenging. Statistically significant multivariable results for food from two studies were discordant in that one found eating chicken protective while eating other poultry was a risk factor [12]. The other found eating chicken or pre-cooked cold meats to be a risk factor [18]. The food handling results were largely protective, but only from univariable analyses [12, 17]. Some risk factors for infection with *Campylobacter* may be independent of the susceptibility of the strain, and interventions that reduce the overall prevalence or concentration of *Campylobacter* in food or water could also reduce the risk of infection with a resistant strain, yet these types of factors were not studied [53-56]. It is also possible that risk factors for infection with a resistant strain would differ if there was more global representation among the studies included in the review, as different antimicrobials may be used and in some areas access to these drugs can be over-the-counter for humans and animals [57, 58]. Lastly, while only one study included a factor related to vegetables [18], antimicrobial use in plant agriculture and the use of manure from animals as a fertilizer for crops may increase the risk of resistant organisms on produce [44, 59, 60].
Water consumption and contact are also recognized as potential risk factors for *Campylobacter* infection [51], however, only four studies reported water-related factors with marked variability in definition and results [12, 17, 18, 24]. Water contamination with *Campylobacter* varies regionally, however, little is known about contamination with fluoroquinolone-resistant versus susceptible *Campylobacter*. Fluoroquinolone resistance is largely mutational in *Campylobacter*, rather than by acquisition through mobile genetic elements [10], meaning that antimicrobial use in humans or animals and selection for resistant strains that contaminate water is the more likely source compared to acquisition in the environment. None of these studies evaluated this potential linkage, which would require more data about antimicrobial use and genomics.

**Overall considerations**

Antimicrobial resistance is a complex, population-level issue across One Health sectors that is driven by individual, regional, and global activities [60]. These studies discussed factors on the individual level, however, population-level influences such as environment sources, cleanliness of water, crop and animal agriculture, the spread of resistant organisms, the overall availability of antimicrobials, and the prescribing nature of the physicians and veterinarians are important to consider [44, 52, 60]. Identified factors and associations with risk of infection with resistant *Campylobacter* were variable and generalizability was largely limited to wealthy, western countries. Resistance does not recognize borders and AMR surveillance in all countries linked to better patient metadata and genomics are needed to better understand these factors such as travel, prior antimicrobial use, food, and water [42]. In addition to individual patient-level factors, population-level research using a One Health approach that includes water quality, food
safety and preparation, and antimicrobial use would expand our knowledge for risk-prevention strategies for infection with resistant Campylobacter [60, 61].

Care was taken to state these factors as associations with increased or decreased risk of infection with a resistant strain. The most common study design (cross-sectional) may suffer from reverse causation [62]. Additionally, when evaluating case-control studies care must be taken when selecting controls to link the factor for AMR and to control bias [54-56, 61]. The cohort study design controls for temporality of events and provides the opportunity to measure multiple outcomes, but it is not well suited for the relatively rare incidence of infection with a resistant strain of Campylobacter [61].

We chose patients infected with antimicrobial-susceptible strains as our comparison group, which was appropriate for our research question to identify risk factors for infection with a resistant strain among all infections, but may have different results and interpretations than comparison to healthy patients [61]. This comparison group may not be advantageous for identifying the strength of association for all risk factors of resistant Campylobacter infections, especially prior antimicrobial use [56]. Case-case-control studies for infection with resistant organisms compare those infected with a resistant strain to those with a susceptible strain and those who are healthy with a negative test, which allows researchers to better control for bias [54].

Our work yielded less insight into the global understanding of factors associated with human infection with antimicrobial-resistant Campylobacter than expected. The dearth of published studies included in our review in any low- and middle-income countries should be a call to action for research funders and government surveillance programs alike [63]. Tackling AMR requires a One Health approach at the global level [60], and the lack of investment, for
example, in AMR surveillance in all but developed countries speaks to the stark gaps present in
global AMR research, surveillance, and understanding. Future use of case-case-control or case-
control-control study designs are preferred to examine factors related to infection with resistant
strains [54]. Conducting and reporting of multivariable analyses is very important as simple
univariable associations fail to account for confounding or identify interactions between related
factors. In addition, reporting of all factors assessed for association, not just those found to be
statistically significant in uni- and multivariable models would provide the complete picture.

Limitations

We aimed to minimize the possibility of not capturing all eligible articles for our review,
a risk inherent in any literature review, by following a rigorous, systematic approach [64]. The
factor list identified in this review is by no means exhaustive, it is likely there are factors that
were outside the scope of our search or for which research is likely lacking. Our protocol also
excluded articles primarily focused on identifying molecular and genetic similarities between
human Campylobacter isolates with AMR with those from other sources such as animals and
water. The synthesis of such literature was beyond the scope of this study but would be an
important future contribution to the understanding of human infection with resistant
Campylobacter. Additionally, excluding non-English articles and publishing bias against null
findings has the potential to influence included factors in our review [14]. There is limited global
generalizability because there were no studies from Africa and South America and 24 out of 27
studies were in westernized, high-income countries. The lack of multivariable results for most
studies, and in particular, a seeming lack of identified or assessed interactions between factors
may fail to capture the complicated, interconnected nature of the impact of multiple factors on
the risk of infection with resistant strains.

Conclusions

This scoping review mapped the current literature that investigated and quantified risk or
protective factors related to a human infection with antimicrobial-resistant *Campylobacter*
compared to susceptible infections. Travel, prior antimicrobial use, food consumption and
handling, water consumption and exposure, and animal contact were important factors associated
with the risk of infection with a resistant strain. The heterogeneity of the results, focus on
fluoroquinolone-resistant outcomes, and lack of multivariable analyses made identifying
concrete associations with risk factors challenging but highlighted areas for potential future
research. The study of AMR in *Campylobacter* would benefit from an interdisciplinary, One
Health research approach that expands to include research in low- and middle-income countries.

Declarations

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Conflicts of Interest
Data Availability Statement

The search protocol and all extracted data are provided in Supplementary Material. All Supplementary Material is available on the Cambridge Core website.

Authors’ Contributions

See the summary included with co-authors in the submission portal.
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Table 1. Key characteristics of peer-reviewed references included in the scoping review of factors related to human infection with an antimicrobial-resistant strain of *Campylobacter* species.

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Location</th>
<th>AMR</th>
<th>Species</th>
<th>Infection Site</th>
<th>Total Sample Size</th>
<th>Age Details</th>
<th>Percent Female</th>
<th>Author and Year</th>
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<tbody>
<tr>
<td>Case Control (n=4)</td>
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<tr>
<td>Denmark</td>
<td>Quinolone, Fluoroquinolone</td>
<td>jejuni</td>
<td>NS</td>
<td>126</td>
<td>Mean = 33, IQR = 20-45</td>
<td>83.3</td>
<td>Engberg J, et al, 2004 [12]</td>
<td></td>
</tr>
<tr>
<td>India</td>
<td>Macrolides, Quinolones, Fluoroquinolones, Tetracyclines</td>
<td>jejuni</td>
<td>GI</td>
<td>400</td>
<td>Mean (cases) = 37, Mean (cont.) = 39.3</td>
<td>41.8</td>
<td>Kownhar H, et al, 2007 [36]</td>
<td></td>
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<tr>
<td>United Kingdom</td>
<td>Fluoroquinolones</td>
<td>NS</td>
<td>NS</td>
<td>556</td>
<td>Med (cases) = 50.7, 53</td>
<td>Evans M, et al, 2009 [17]</td>
<td></td>
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<tr>
<td>Study design</td>
<td>Location</td>
<td>AMR</td>
<td>Species</td>
<td>Infection site(^b)</td>
<td>Total sample size</td>
<td>Age details ((\text{years})^c)</td>
<td>Percent female(^d)</td>
<td>Author and year</td>
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<tr>
<td>Case-Case-Control ((n=1))</td>
<td>France</td>
<td>Fluoroquinolones</td>
<td><em>jejuni, coli, fetus, lari</em></td>
<td>GI</td>
<td>570</td>
<td>Mean (cases) = 0</td>
<td>Gallay A, et al, 2007 [20]</td>
<td></td>
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\(^a\) Med (comp.) = 49

\(^b\) GI

\(^c\) Mean (cases) = 19.5

\(^d\) Mean (cont.) = 20
<table>
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<tr>
<th>Study design¹</th>
<th>Location</th>
<th>AMR</th>
<th>Species</th>
<th>Infection siteᵇ</th>
<th>Total sample size</th>
<th>Age details (years)ᶜ</th>
<th>Percent femaleᵈ</th>
<th>Author and year</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Range = 27-53</td>
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<tr>
<td>Australia</td>
<td>Fluoroquinolones</td>
<td><em>jejuni, coli</em></td>
<td>GI</td>
<td>2491</td>
<td>Med. range = 0-6</td>
<td>NS</td>
<td>Uzunovic-Kamberovic S, et al, 2009 [41]</td>
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<tr>
<td>Bosnia and Herzegovina</td>
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<td>Range = 0-64+</td>
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<td>NS</td>
<td>210</td>
<td>16+</td>
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<td>Johnson, J et al, 2008 [21]</td>
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¹ Study design information not shown in the table.

ᵇ Infection site: GI = Gastrointestinal.

ᶜ Age details: Mean = average age, Range = age range.

d Percent female.
<table>
<thead>
<tr>
<th>Study design&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Location</th>
<th>AMR</th>
<th>Species</th>
<th>Infection site&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Total sample size</th>
<th>Age details (years)&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Percent female&lt;sup&gt;d&lt;/sup&gt;</th>
<th>Author and year</th>
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<tr>
<td>Denmark</td>
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<td><em>jejuni</em></td>
<td>NS</td>
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<td>NS</td>
<td>NS</td>
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<td>GI</td>
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<td>NS</td>
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<td><em>jejuni</em></td>
<td>GI</td>
<td>354</td>
<td>NS</td>
<td>NS</td>
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<td>Hakanen A, et al, 2003 [29]</td>
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<td>Ireland</td>
<td>Fluoroquinolones</td>
<td>15 <em>jejuni</em>, 2 <em>coli</em></td>
<td>GI</td>
<td>15</td>
<td>Mean = 29.4</td>
<td>26.7</td>
<td>Moore J, et al, 2002 [40]</td>
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<sup>a</sup> Study design

<sup>b</sup> Infection site

<sup>c</sup> Age details

<sup>d</sup> Percent female
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<tr>
<th>Study design&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Location</th>
<th>AMR</th>
<th>Species</th>
<th>Infection site&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Total sample size</th>
<th>Age details (years)&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Percent female&lt;sup&gt;d&lt;/sup&gt;</th>
<th>Author and year</th>
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<tr>
<td>Netherlands</td>
<td>Macrolides, Fluoroquinolones, Tetracyclines</td>
<td>94% <em>jejuni</em></td>
<td>NS</td>
<td>18856</td>
<td>NS</td>
<td>NS</td>
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<td>van Hees B, et al, 2006 [33]</td>
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<td><em>jejuni</em></td>
<td>GI</td>
<td>174</td>
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<td>40.2</td>
<td>Ghunaim H, et al, 2015 [28]</td>
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<td><em>jejuni</em></td>
<td>GI</td>
<td>495</td>
<td>Mean (cases) = 39</td>
<td>52.3</td>
<td>52.3</td>
<td>CSSSC e, et al, 2002 [18]</td>
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<td>GI/BS</td>
<td>16549</td>
<td>Med. = 38</td>
<td>45.0</td>
<td>Patrick M, et al, 2018 [31]</td>
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<td>Study design&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>AMR</td>
<td>Species</td>
<td>Infection site&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>Age details (years)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Percent female&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Author and year</td>
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<td>WonHee C, et al, 2016 [65]</td>
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<td>Macrolides</td>
<td>Mostly <em>jejuni</em></td>
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<td>Mean (cases) = 37.1</td>
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<td>Ricotta E, et al, 2014 [34]</td>
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**Cohort (n=2)**
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<th>Study design&lt;sup&gt;a&lt;/sup&gt;</th>
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<th>AMR</th>
<th>Species</th>
<th>Infection site&lt;sup&gt;b&lt;/sup&gt;</th>
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<th>Age details&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Percent female&lt;sup&gt;d&lt;/sup&gt;</th>
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<tr>
<td></td>
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<td>Retrospective Cohort (n=3)</td>
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<td>Age details (years)</td>
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<td>Range = 21-64</td>
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<td>Gaudreau C, et al, 2015 [38]</td>
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<td>Range = 4-81</td>
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</tbody>
</table>

*a* When a study design was not specified by the authors, the study design was determined by the first author during data extraction based on the reported methods.

*b* Infection type specified or determined during data extraction where possible, GI=Gastrointestinal Infection, BS=Blood-stream infection, NS=not specified/could not be determined.
Specified or calculated during data extraction where possible, IQR= interquartile range, Med.=median, cont.=controls, comp.=comparisons, NS=not specified

%d female vs other, specified in article or calculated during data extraction where possible, NS=not specified

CSSSC = Campylobacter Sentinel Surveillance Scheme Collaborators
Figure 1. PRISMA scoping review flow diagram of the study selection process for the scoping review of human infection with an antimicrobial-resistant strain of *Campylobacter* species.
Figure 2. Animal contact factors identified in studies included in the scoping review for human infection with antimicrobial-resistant *Campylobacter* compared to infection with susceptible strains, limited to studies reporting odds ratios. UVA – univariable analysis result. MVA – multivariable analysis result.

Figure 3. Prior antimicrobial use as factors identified in studies included in the scoping review for human infection with antimicrobial-resistant *Campylobacter* compared to infection with susceptible strains, limited to studies reporting odds ratios.

Footnote. UVA – univariable analysis result. MVA – multivariable analysis result. UVA* - results from a study that only conducted univariable analysis. F – fluoroquinolone resistant outcome. Q – quinolone resistant outcome.
Figure 4. Food consumption (A) and preparation (B) factors identified in studies included in the scoping review for human infection with antimicrobial-resistant *Campylobacter* isolates compared to infection with susceptible strains, limited to studies reporting odds ratios.

Footnote. UVA – univariable analysis result. MVA – multivariable analysis result. F fluoroquinolone resistant outcome. CSSSC – *Campylobacter* Sentinel Surveillance Scheme Collaborators.
Figure 5. Travel factors identified in studies included in the scoping review for human infection with antimicrobial-resistant *Campylobacter* isolates compared to infection with susceptible strains, limited to studies reporting odds ratios.

Footnote. UVA – univariable analysis result. MVA – multivariable analysis result. UVA* - results from a study that only conducted univariable analysis. F – fluoroquinolone resistant outcome. Q – quinolone resistant outcome. CSSSC – *Campylobacter* Sentinel Surveillance Scheme Collaborators.
Figure 6. Key data extracted for drinking water-related (A) and swimming (B) factors identified in studies included in the scoping review for human infection with an antimicrobial-resistant *Campylobacter* isolates compared to infection with susceptible strains, limited to studies reporting odds ratios.

Footnote. UVA – univariable analysis result. MVA – multivariable analysis result. UVA* - results from a study that only conducted univariable analysis. F – fluoroquinolone resistant outcome. Q – quinolone resistant outcome. CSSSC – *Campylobacter* Sentinel Surveillance Scheme Collaborators.