# PROJECT UPDATE – Work Package 3B

# Human Exposure to and Risk from Antimicrobial-resistant *Campylobacter, Enterococcus* and ESBL-producing *E. coli*: A Farm-to-Fork Assessment


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## INTRODUCTION:

We must understand the magnitude of foodborne antimicrobial resistance (AMR) risks to design One Health antimicrobial stewardship approaches for veterinary and human medicine. This project is focused on quantitative modeling strategies to understand the risk of AMR transmission through the food chain to people. Two primary research questions are:

**1) What is the human exposure to and risk of foodborne transmission of antimicrobial-resistant *Campylobacter*?**

2) What is the human exposure to foodborne transmission of AMR from beef cattle (using the macrolide-resistant indicator *Enterococcus* spp. & extended-spectrum beta-lactamase (ESBL)-producing *E. coli)*? (Collaborative linkages to Work Package 3A and 3C - see posters for details.)

## METHODS:

**Scoping Review** | **Integrated Assessment Model** | **Quantitative Microbial Risk Assessment Framework** (Novel Dose Response Model)

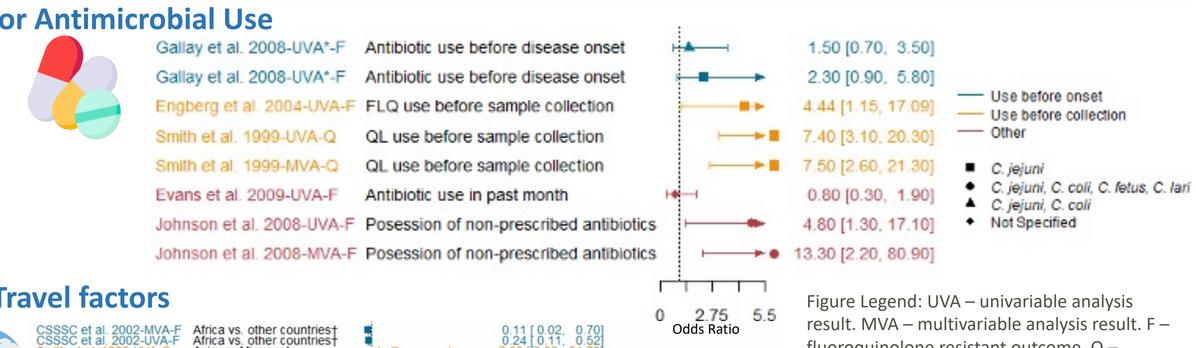
## SCOPING REVIEW[1]:

**Followed Joanna Briggs Institute & PRISMA guidelines[2] to answer the research question: What factors are associated with an antimicrobial-resistant *Campylobacter* infection in humans?**

- Databases searched: ProQuest® AGRICOLA, CAB Abstracts® and Global Health®, Ovid EMBASE®, Scopus®, Ovid MEDLINE® + 3 Grey literature sources
- Key search themes included: *Campylobacter,* antimicrobials, and antimicrobial resistance
- Screening by two independent reviewers
- Inclusion criteria: analytical study; available in English; infection confirmed by laboratory diagnostic methods; human exposure to factors potentially associated with *Campylobacter* strain resistant to macrolides, tetracyclines, quinolones, or fluroquinolones; comparator group appropriate for study design (E.g. for case-control studies comparator group = infections with strains of *Campylobacter* susceptible to antimicrobials of interest)
- The search was completed on February 5, 2020 and updated on May 7, 2021
- Factors were categorized into:
  1. animal contact,
  2. prior antimicrobial use,
  3. participant characteristics,
  4. food consumption and handling,
  5. travel,
  6. underlying health conditions,
  7. water consumption/exposure.

8541 records identified through search strategy
↓
8527 records after duplicates removed
↓
8089 records removed during title and abstract screening
↓
411 records removed during full text screening
↓
**27 articles included**

### Prior Antimicrobial Use




### Travel factors

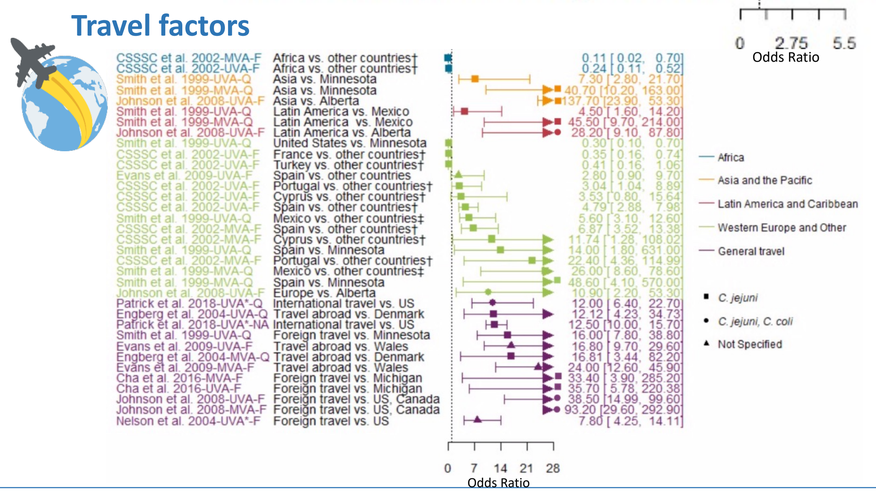



Figure Legend: UVA – univariable analysis result. MVA – multivariable analysis result. F – fluoroquinolone resistant outcome. Q – quinolone resistant outcome.

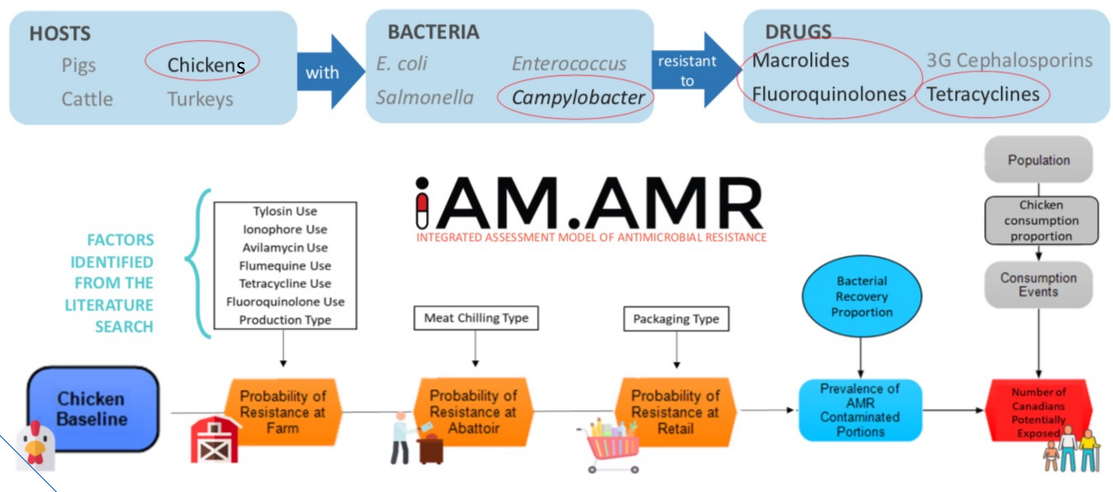
### TAKEAWAYS:

- Heterogeneity of the results and factor definitions provided a **broad overview**
- Factors linked to **increased likelihood of infection** with a fluoroquinolone-resistant strain included **foreign travel** and **prior antimicrobial use**.
- Future research using an **interdisciplinary, One Health approach** is needed to prioritize important risk factors.

## INTEGRATED ASSESSMENT MODEL[3]:

### The iAM.AMR Project & Modelling Scenarios

The Integrated Assessment Model for Antimicrobial Resistance (iAM.AMR) aims to use disparate data sources to describe the potential for factors to alter human exposure to resistant bacteria along the farm-to-fork pathway. We used this model to answer the research question: **What is the number of Canadians potentially exposed to antimicrobial-resistant *Campylobacter* from chickens and their meat in Canada account for factors from farm to retail?**




### STEPS:

1: Literature Search → 15 articles from scoping review (designed and executed by the iAM.AMR team) included in quantitative synthesis

2: Determining the baseline → Defined as the likelihood a pre-placement chick in Canada will be colonized with AMR *Campylobacter* without any specific intervention

3: Factors → Farm, Abattoir, and Retail

4: Modeling → Overall probability of *Campylobacter* having a particular drug resistance at each node is calculated with a stochastic process using Median Latin Hypercube sampling to determine the uncertainty of the final outcome

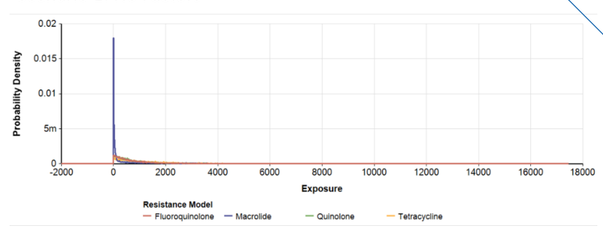
### RESULTS:

Estimated **number of people (per 100,000) exposed** to antimicrobial-resistant *Campylobacter* from chicken:

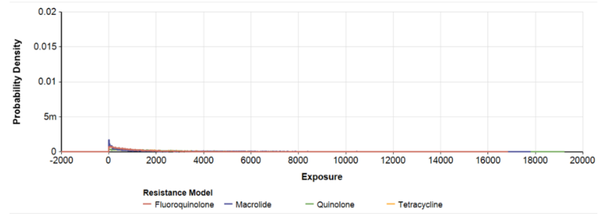
| | No Factors | Canadian Factors |
|---|---|---|
| FLQ-R | 611.19 | 965.12 |
| MAC-R | 101.71 | 1,721.47 |
| QL-R | 613.05 | 1,915.63 |
| TET-R | 986.10 | 1,805.15 |

Figure legend: FLQ-R – Fluroquinolone resistant. MAC-R – Macrolide resistant. QL-R – Quinolone resistant. TET-R - Tetracycline resistant.

Scenario 1: No Factors




Scenario 2: Canadian context




### TAKEAWAYS:

- **Antimicrobial use**, **unconventional production**, **immersion chilling**, and **unpackaged sales increase estimated exposure**
- **Persistent estimated exposure to FLQ-R** *Campylobacter* from chicken despite decreasing FLQ use on-farm
- Large **data gaps** in prevalence of resistant *Campylobacter* at chick placement and factor data, particularly a lack of any Canadian factor data from the literature

## QUANTITATIVE MICROBIAL RISK ASSESSMENT (QMRA)[4]:

**QMRA framework (outlined below) was used to answer the research question: What is the risk of treatment-resistant illness to Canadians from retail chicken meat?**

**Hazard Identification:**
**Chickens on the farm:**
22% of samples are *Campylobacter*[2], and 13.11% of these are Ciprofloxacin-resistant (CIPR)[5]
**Chickens (retail):**
25.4% of samples are *Campylobacter*[5], and 13.59% of these are CIPR[5]
**Humans:**
Approximately 24% of lab confirmed cases are CIPR[6]

Hazard Characterization
Exposure Assessment
Risk Characterization

Novel Dose-response model. More[7] info here:

Novel model (from Chandrasekaran & Jiang)[8]:

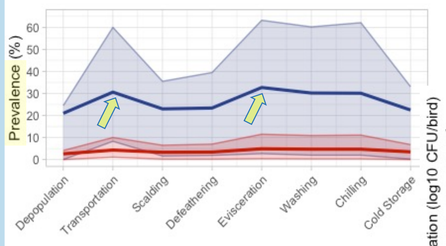
$$P_{inf} = 1 - \left(1 + \left(\frac{d \times f_r}{\beta_R}\right)\right)^{-\alpha_R} \times \left(1 + \left(\frac{d \times (1 - f_r)}{\beta_S}\right)\right)^{-\alpha_S}$$

### Exposure assessment along the farm to fork pathway:

1. Depopulation
2. Transportation
3. Scalding
4. Defeathering
5. Evisceration
6. Washing
7. Chilling
8. Cold storage
9. Home preparation

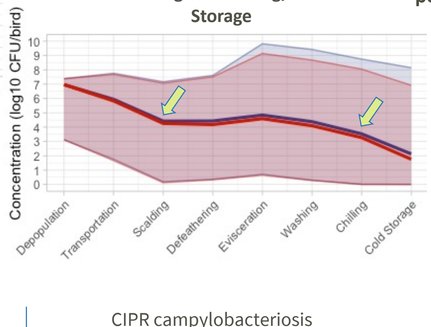
**To determine:**
- Probability any random serving of chicken has CIPR or any *Campylobacter*
  …and if it does…
- Dose of CIPR *Campylobacter* and/or total *Campylobacter*

### Farm-to-fork estimates:




Spikes in prevalence at **Transportation** and **Evisceration**

Concentration reductions at **Scalding** and **Chilling/Cold Storage**




### Estimates of risk:

| | Campylobacteriosis | | | CIPR campylobacteriosis | | |
|---|---|---|---|---|---|---|
| Individual serving | 0.000082% (5th percentile) | 0.015% (Median) | 3.1% (95th percentile) | 0.000012% (5th percentile) | 0.002% (Median) | 0.44% (95th percentile) |
| Population | 6 (5th percentile) | 1,101 per 100,000 (Median) | 223,000 (95th percentile) | 1 (5th percentile) | 143 per 100,000 (Median) | 31,500 (95th percentile) |

### Model Analyses:

**1) Sensitivity Analysis** → Which **data inputs** from exposure assessment are most influential on determining **risk per serving** (total and CIPR)?

- Internal temperate after cooking
- Probability of within-flock contamination during transportation
- Amount of cross-contamination at evisceration

**2) Scenario Analysis** → If **hypothetical changes** were made along farm-to-fork pathway, what would be the outcome in **risk in the population** (total and CIPR)?

- 90% reduction in flock/meat prevalence leaving abattoir → **~97.5% less total illness**
- 90% reduction in mishandling at home → **~90% less total illness**
- 50% reduction in flock prevalence at the farm → **~50.5% less total illness**

### TAKEAWAYS:

- Model estimates **143** per **100,000** (approx. 53,648) Canadians will experience CIPR campylobacteriosis/ year
- **Data gaps** limited ability to quantify CIPR *campylobacter* along the farm to fork pathway
- CIPR *Campylobacter* is persistent, and to protect human health **development and evaluation of targeted control strategies** is needed.


Public Health Agency of Canada | Agence de la santé publique du Canada
Agriculture and Agri-Food Canada | Agriculture et Agroalimentaire Canada
Alberta Government
UNIVERSITY OF CALGARY



References:
[1]Neustaedter, C.N., et al. 2022. Factors associated with antimicrobial-resistant *Campylobacter* species infections in humans: A scoping review. [Poster]. ISVEE, August 2022, Halifax, N.S.
[2]Aromataris E, Munn Z. JBI manual for evidence synthesis [Internet]. Australia: JBI; 2020 (https://synthesismanual.jbi.global)
[3]Neustaedter, C.N., Tschritter, D., et al. 2022. Modeling antimicrobial-resistant *Campylobacter* spp. in broiler chicken in Canada using an integrated assessment model. [Poster]. ISVEE, August 2022, Halifax, N.S.
[4]Tschritter, D., et al. 2022. Farm-to-fork QMRA of ciprofloxacin-resistant *Campylobacter* from chicken meat in Canada. [Presentation]. ISVEE, August 2022, Halifax, N.S.
[5]Public Health Agency of Canada. *Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) 2018: Figures and Tables*. Guelph, ON: 2020.
[6]Inglis G. *et al.* Rates of fluoroquinolone resistance in domestically acquired *Campylobacter jejuni* are increasing in people living within a model study location in Canada. *Can J Microbiol*. 2021;67(1):37-52. doi: 10.1139/cjm-2020-0146.
[7]Tschritter, D., et al. 2022. A novel dose-response model for infection with ciprofloxacin-resistant *Campylobacter.* [Poster]. ISVEE, August, 2022, Halifax, N.S.
[8]Chandrasekaran S, Jiang SC. A dose response model for quantifying the infection risk of antibiotic-resistant bacteria. *Scientific Reports*. 2019;9:17093. doi: 10.1038/s41598-019-52947-3.