Comparing 'source attribution' models for human campylobacteriosis.

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Summary

• New Zealand has one of the highest notification rates for human campylobacteriosis in the developed world.
• National policy setting relies on good information about the origin of these cases.
• *Campylobacter jejuni,* the primary cause, is isolated from multiple food and environmental sources.
• We compare three modelling approaches to apportion human cases to different sources, using genotyping data.
• All three methods give broadly similar results.
• Poultry was identified as a primary source of human infection in New Zealand.
• This information has been valuable for targeting national control strategies.

Introduction

• In New Zealand the reported rate of human campylobacteriosis rose to a peak of 16,000 cases (400/100,000) in 2006[1,2].
• In order to control the campylobacteriosis epidemic, the regulator – the New Zealand Food Safety Authority – need to know which were the predominant pathways for human infection.
• Earlier 'source attribution' studies, based on case control studies and pathway simulation, indicated that fresh poultry was a major source[3].
• In this study we adapt two models, previously used to apportion salmonellosis cases to food sources[4], and apply them to *C. jejuni* genotyping data.
• We add a third approach, based on population genetics, and compare all three techniques for attributing both food and environmental pathways to human cases.

Methods: data collection and genotyping

• The study area was the Manawatu region of North Island, New Zealand. All isolates were taken from this area.
• Samples from human clinical cases, food, recreational waters and livestock and wildlife faeces were cultured using standard techniques. Inoculated Bolton's broths were incubated at $42°C$, microaerobically for 48 hours then plated onto mCCDA agar for 48 hours at $42°C$.
• Multilocus Sequence Typing (MLST) was performed as described by Dingle et al., 2001[5]
• Models fitted for 263 human cases assigned to genotypes between Nov 2004 and March 2007. Isolates from other sources included poultry (N=254), cattle (N=35), sheep (N=63), environmental water (N=25) and wild birds (N=23).

Manawatu

Methods: source attribution models

Model 1: the 'Dutch' model
Estimates number of cases without uncertainty (deterministic)
No account taken of relative exposure / food source factors.

$$\lambda_{ij} = \frac{p_{ij}}{\sum_j p_{ij}} x_i$$

$$\lambda_j = \sum_i \lambda_{ij}$$

Where:
λ_{ij} = estimated number of human cases of type i attributable to source j
p_{ij} = proportion of type i in source j
x_i = number of human cases of type i

Model 2: the adapted 'Danish' model
Estimates number of cases with measure of uncertainty using Bayesian inference.

$$\lambda_{ij} = p_{ij} a_j q_i$$

Where:
p_{ij} = matrix of prevalence of different strain types
a_j = relative 'danger' of food or environmental sources.
q_i = relative 'virulence' of strains.

Model 3: the 'Island' model
Estimates number of cases by estimating probability that individual strain types originated in each source.
Based on population genetics and 'coalescent' model of genealogy of *C. jejuni*.
Animal populations considered 'islands'; mutation and horizontal gene transfer rates estimated from MLST data.
Gene flow 'migration' from these sources to humans used to estimate source attribution.
Provides estimates of uncertainty and can assign strains only found in humans.

Results

• One strain known as Sequence Type ST-474 accounted for ~25% of human cases and was commonly isolated from poultry. ST-474 is rare in other countries.
• Both poultry and ruminant-associated strains were isolated from humans.
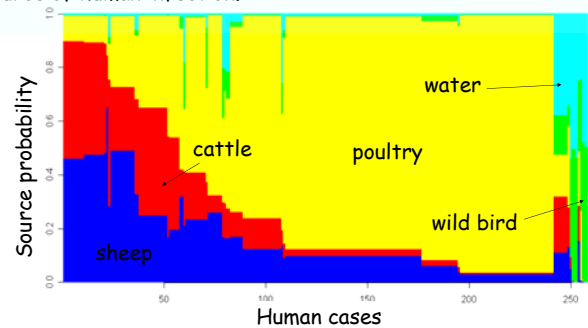• All three models indicated poultry was the single most important source of human infection.

Figure 1. Matrix plot of source probability for 263 human cases. Isolates ordered to aid visualisation.

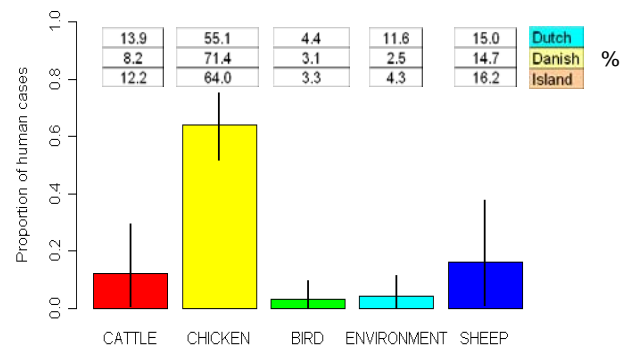| 13.9	55.1	4.4	11.6	15.0	Dutch
8.2	71.4	3.1	2.5	14.7	Danish
12.2	64.0	3.3	4.3	16.2	Island

%

Figure 2. Estimated proportion of human cases arising from each source showing output from the 'Island' model (bar chart with 95% credible intervals) and the 'Dutch' and 'Danish' models of New Zealand data (Boxes above bar chart showing %).

Discussion and conclusions

• Studies in Auckland and Christchurch have also shown a similar pattern of strain types in humans and poultry.
• Source attribution models based on molecular genotyping have proved valuable for identifying the most likely sources of human campylobacteriosis in New Zealand.
• They have contributed to the implementation of the *Campylobacter* In Poultry Risk Management Strategy 2007-10[6].
• Early indications suggest this has coincided with a rapid decline in the number of human cases.
• These techniques require typing tools that identify host associated strains. This may not apply in all countries, where other methods for source attribution may be more appropriate.

References: **1.** Baker, M. et al. 2006. N Z Med J 119, 2264. **2.** Baker, M.G. et al 2007, Epidemiol Infect 135, 163-170. **3.** Dingle, K.E. et al. 2001. J Clin Microbiol 39, 14-23.
4. Eberhart-Phillips, J. et al. 1997. J Epidemiol Community Health 51, 686-691. **5.** Hald, T. et al. 2004. Risk Anal 24, 255-269.
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