



Campylobacter in Food and the Environment:

Examining the Link with Public Health

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***Campylobacter* in Food and the Environment: Examining the Link with Public Health**

May 2011

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EXECUTIVE SUMMARY

Recognising the importance of the burden of campylobacteriosis and possible links with microbial contamination of New Zealand environmental waters, the New Zealand Food Safety Authority and the Ministry for the Environment (with support-in-principle from the Ministry of Health), obtained a research grant from the Cross Departmental Research Pool (CDRP)¹ to be carried out by a multi-agency team to conduct a three-year research programme on "*Campylobacter* in food and the environment: examining the link with public health". This grant recognized that a number of strands of relevant work had been reported and were in progress, such that adopting a more holistic approach, via modelling, was likely to bear fruit—indicating how interventions might affect food safety and environmental outcomes while taking account of data availability. It also recognized that new and emerging microbiological techniques, when married with modelling approaches, held the promise of substantially enhanced predictive power, particularly in their ability to separate different sources of this bacterium. Funding for this project ceased at the end of June 2010.

The main outputs from the project are the following models:

- source attribution, using genotype information (Massey)
- pathway attribution, including various exposures (ESR)
- carriage and transmission by farmed animals (Massey)
- catchment dynamics and associated risk model (NIWA).

These models have been fully documented in five separate agency reports, and the models themselves have been delivered to the Ministry of Agriculture and Forestry (the New Zealand Food Safety Authority has recently been amalgamated with that Ministry). The food-related models can be used at national or health district scale, but the environmental models generally apply to the catchment scale.

These models can now be used by other investigators. They have been linked to assist the compiling of the merits of interventions and mitigations in food and environmental systems in different catchments. While the accompanying technical reports² make some study of the potential benefits of possible interventions, we have not generally recommended which of them could be best adopted, because a number of other factors may also need to be considered. Also, a paucity of *Campylobacter* data for environmental systems means that there is limited confidence in some model outcomes.

In developing and using these models we have found that:

1. The source attribution and pathway models have shown that while the poultry component has declined (given the interventions already undertaken), poultry is still a significant part (as much as one half) of the overall attribution and so further risk management may prove beneficial in terms of burden reduction.

¹ The CDRP fund was administered by the Foundation for Research Science and Technology (FRST) on behalf of Ministry of Research Science and Technology (MoRST).

² Elliott (2011), Elliott & Harper (2011), French *et al.* (2011), Lake *et al.* (2011), Marshall & French (2011).

2. Human campylobacteriosis cases in the Manawatu attributed to cattle and sheep in 2008 exceeded those attributed to poultry (the Manawatu is a comparatively data-rich region). These findings were obtained using two different models which were informed by strain-typing funded in part funded by this project.
3. The pathway model has shown that the individual contributions of a number of risk factors to the total predicted disease burden are relatively small. These have been categorised as: occupational exposure, exposures for 0-4 year olds living in a rural environment, overseas travel, person-to-person contact, contact with cats and dogs, red meat and offal, and recreational water exposure.
4. Based on data from notified cases, there is a higher risk of illness amongst 0-4 year olds living in a rural environment, compared to those children living in urban environments.
5. The pathway modelling has identified a “remainder” proportion of the attribution that cannot currently be assigned. This remainder will include a variety of exposures, including those from drinking water, as well as “other” animal contact (i.e., excluding animal contact already addressed by the model), and consumption of other foods such as unpasteurised milk.
6. The exploration of available data (by this project) to populate an exposure model for drinking water has revealed a shortage of information on key inputs, particularly:
 - Populations served by unregistered water supplies
 - Water sources and treatment status of such unregistered supplies
 - Frequency of exposure to drinking water outside of the normal home supply (e.g. exposures for urban populations during camping trips, farm visits etc.)
7. The environmental models, aided by further strain typing of isolates from river water during flood flows (funded by DairyNZ), confirm that *Campylobacter* concentrations during low flow periods are usually low and are dominated by wild bird species. However during flood periods concentrations become much higher, are dominated by ruminant species, and this is the result of local runoff from farmed areas.
8. Information is still lacking on the relative importance of surface washoff of *Campylobacter* versus infiltration flow contaminant pathways from faecal deposits on the land to waterways (identified in the findings of the earlier CDRP-funded project "Pathogen Transmission Routes Research Programme").

1 INTRODUCTION

Campylobacteriosis is New Zealand's most frequently reported zoonosis.³ Its reported rate peaked in 2006 at 383 cases of illness per 100,000 people per annum, four-fold higher than the combined reported rates for the other three major notifiable zoonoses (cryptosporidiosis, giardiasis, and salmonellosis).⁴ Despite recent reductions, the reported rate remains high compared to other developed countries. In 2009 the reported rate was 166.3 per 100,000 population, which is higher than the most recent reported rates in Australia, of 108 per 100,000 in 2008, and 72 per 100,000 in 2009.⁵ However differential under-reporting between countries can mask the true differences.

This issue has been a matter of general concern and considerable resources have been allocated to its investigation.

Campylobacteriosis principally presents as acute gastrointestinal illness, with low rates of mortality and sequelae. Not all cases will present to a general practitioner, and consequently the *reported* rate (notified cases) is much less than its *actual* rate.⁶ The best estimate (from a UK study) is that the latter is about an order of magnitude higher than the reported rate. Furthermore the efficacy of reporting systems varies between countries, thus confounding comparisons between New Zealand's reported rate and those of other countries (many countries do not even have a reporting system for campylobacteriosis).

Contaminated food, particularly poultry, is considered to be one of the main human exposure pathways, so the New Zealand Food Safety Authority (NZFSA) has a vital interest in managing that risk. The NZFSA *Campylobacter* Risk Management Strategy describes research and interventions in support of that aim. At the same time, the Ministry for the Environment (MfE) has a strong interest in improved understanding of microbial aspects of water quality in relation to suitability for recreation and drinking-water sources.

The major "reservoirs" of *Campylobacter* are in farmed animals and wildlife. Human disease-causing environmental exposures could therefore arise by direct contact with animals, contact with contaminated water during recreational activities, or consumption of contaminated drinking-water.⁷ There could also be "knock on" effects whereby exposure to contaminated food was caused by transmission of *Campylobacter* from the environment to food production and processing systems. Therefore, it may be mistaken to confine investigations of intervention measures

³ Zoonoses are "... diseases and infections (the agents of) which are naturally transmitted between vertebrate animals and man" (WHO/FAO 1959).

⁴ These reported diseases rates are readily available through the Public Health Observatory (<http://www.nzpho.org.nz/NotifiableDisease.aspx>)

⁵ http://www9.health.gov.au/cda/source/Rpt_2.cfm?RequestTimeout=500

⁶ The many reasons for this state of affairs are often described via the "reporting pyramid" (e.g., Lake *et al.* 2010). Layers in this pyramid depict all the necessary steps that must be taken before it is possible to report incidence. For example, an ill person must visit a doctor who must request that a stool sample be supplied and analysed for the presence of *Campylobacter*, an infected stool is later supplied and analysed correctly, and a positive result must be entered into the reporting system. If any one of these steps is not fulfilled, the case will not be reported.

⁷ Potential public health risk of waterborne zoonotic pathogens in New Zealand is presented by Till & McBride (2004).

aimed at reducing this disease burden just to food production and preparation.⁸ Interventions closer to the environmental sources of *Campylobacter* may also need to be considered, especially if those sources can be shown to contain strains that are particularly pathogenic to humans. Furthermore, reducing the environmental load of *Campylobacter* would likely result in cleaner environmental waters, including drinking water sources. Concern about environmental contamination was such that by 2006 (when reported campylobacteriosis rates peaked) the Ministries of Environment and Health had already promoted new microbiological water quality guidelines for freshwaters (MfE/MoH 2003). These were based on a risk analysis for *Campylobacter* infection in recreational water users, after a national microbiological survey (the Freshwater Microbiological Research Programme, conducted in 1998-2000) had determined that *Campylobacter* was often present in recreational waters—sometimes in high concentrations (McBride *et al.* 2002, Till *et al.* 2008).

Recognising these issues, in 2007 the New Zealand Food Safety Authority and the Ministry for the Environment, with support-in-principle from the Ministry of Health, sought and obtained a three-year research grant from the Cross Departmental Research Pool (CDRP).⁹ The title of that grant is "*Campylobacter* in food and the environment: examining the link with public health". This grant recognized that a number of strands of relevant work had been reported and were in progress, such that adopting a more holistic approach, via modelling, was likely to bear fruit, particularly to identify effective interventions in food production and processing systems—the Food Safety Authority's main interest—and environmental interventions. The latter is of particular interest to the Ministry of Health and the Ministry for the Environment given the latter's role in implementing the National Environmental Standard for Sources of Human Drinking water, which focuses on improved management of drinking water sources in order to reduce the risk of contamination of water supplies prior to treatment. These Ministries also have an interest in decreasing environmental microbial contamination of recreational water (as do regional and district government agencies).

Modelling was seen as a means of pulling various strands of work together in a quantitative way. Furthermore, the now-defunct Enteric Zoonotic Disease Research Group had set up a Modelling Group which forms the core of the current research team.

At the same time, new microbiological techniques for identifying many distinct strains of *Campylobacter* were being developed abroad and in New Zealand, adding considerable power to our ability to differentiate sources of this pathogen, and enhancing the case for the proposed modelling research. Multilocus sequence typing (MLST) of isolates has been used to examine the contribution that different sources of *Campylobacter* make to the overall human health burden. Information on the strains that occur in both sources and human cases of campylobacteriosis can be used to scale the attribution of human health burden to sources and pathways of exposure.

⁸ Here we use mitigation and intervention interchangeably. They both refer to measures which would be introduced to reduce risks or effects. The former tends to be used more in water quality management while the latter tends to be used more in a medical or veterinary context.

⁹ The CDRP was at that time administered by the Foundation of Research, Science and Technology.

The main outputs from this project are the following models:

- source attribution, using genotype information (Massey)
- pathway attribution, including various exposures (ESR)
- carriage and transmission by farmed animals (Massey)
- catchment dynamics and associated risk model (NIWA).

These models are only briefly described in this report. Elaboration of their detail, assumptions, data, construction, operation and output is described in accompanying technical reports (Elliott 2011, Elliott & Harper 2011, French *et al.* 2011, Lake *et al.* 2011, Marshall & French 2010) and papers (McBride 2011, McBride & Chapra 2011, McBride & French 2010). They can be used by operational and policy agencies to investigate pathways and potential interventions. In doing so some familiarity with modelling techniques would be necessary.

This project has made preliminary examinations of potential interventions and these illustrate how the models can inform such an evaluation. We would expect that a detailed evaluation of such factors as: underlying assumptions, confidence in model predictions, costs and benefits would be required for risk management decision making.

2 THE CURRENT SCENE

Indications are that the reduction in the reported rate of campylobacteriosis between 2006 and 2009 reflects a real and substantial reduction in the actual rate.¹⁰ A large part of this decrease is attributable to reduced contamination of fresh poultry meat—contemporaneous analysis of MLST *Campylobacter* strains found in human cases, poultry, cattle, sheep and environmental water samples in the Manawatu supports this inference (French *et al.* 2011). The proportion of cases attributable to consumption of contaminated poultry has dropped from a peak of around 70–75% in 2006 to 30–50% in mid 2010 (French & Marshall 2010, Sears *et al.* 2011). Consequently, exposures from other sources have become of greater interest.

2.1 Basic understandings of *Campylobacter* in the environment

In developing models (see below), we have used some particular understandings regarding environmental *Campylobacter*, as follows:

- (i) There is widespread occurrence of *Campylobacter* in waterways (Till *et al.* 2008). This is attributable to its high prevalence in animal groups, and not because of its environmental persistence—in fact it is much more susceptible to inactivation outside its animal host than most waterborne or foodborne pathogens and indicators (including the frequently-measured *E. coli* indicator bacterium). Alexander & McBride (2011), applying regional-scale statistical models to data obtained from the Freshwater Microbiological Research Programme, report large differences in the sizes of upstream source areas that contribute to varying percentages of the *Campylobacter* and *E. coli* loads at watershed outlets. Hence the effective upstream contributing area for *Campylobacter* is considerably smaller than that area for *E. coli*.
- (ii) Strain typing is able to distinguish probable *Campylobacter* sources between poultry, ovine, bovine and water birds. This is a powerful new addition to the arsenal available to modelers.
- (iii) Although not conclusive, there is epidemiological evidence of differential human-infectivity between strains, supported by experimental evidence of differential infectivity in animal models and cell culture.
- (iv) *Campylobacter* concentrations in baseflows are generally low (compared with flood flows), and may be dominated by wildfowl sources that pose very limited threat to human health (McBride *et al.* 2009, French *et al.* 2010). In pastoral areas, animal defecation directly into waterbodies may occasionally contribute significantly to baseflow concentrations.
- (v) *Campylobacter* concentrations during higher river flows are generally elevated, and are dominated by bovine and ovine sources, probably derived from faecal material deposited on the ground. This is consistent with interpretations of timing of *Campylobacter* delivery during storms (McBride 2011).
- (vi) The two preceding observations lead to a conclusion that current water quality microbiological guidelines may be based on a somewhat over-estimated human health risk for campylobacteriosis for recreational activities (which generally occur during low flows).

¹⁰ For example, an overall decrease in the associated hospitalisation rates for campylobacteriosis is remarkably consistent with the pattern of reduction of reported rates of campylobacteriosis (Sears *et al.* 2011).

- (vii) The few data available indicate that concentrations of *Campylobacter* in groundwater are generally low, except in locations with flood irrigation (Close *et al.* 2010). While this may be expected to be generally true, further data would be needed for confirmation.
- (viii) Whereas a considerable portion of *E. coli* appearing in streams during floods is "mined" from the stream sediments (having been deposited there during preceding low flow conditions), there is little evidence of such mining occurring for *Campylobacter* (stream sediments tend to be depauperate in *Campylobacter* but rich in *E. coli*, Stott *et al.* 2011).
- (ix) The *Campylobacter* cycle within the poultry production system is largely independent of contamination of the water and land environment, with the possible exception of genotype ST45 which shows strong seasonal variation and is prevalent in multiple animal hosts, including wildlife.

2.2 Basic understandings of *Campylobacter* in food production

- (i) *Campylobacter* in foods result from faecal contamination, particularly during primary processing, and consequently occur on the surface of products (apart from offal).
- (ii) *Campylobacter* is readily destroyed by cooking.
- (iii) Exposures to *Campylobacter* from food are often indirect, via cross contamination to other foods and surfaces (e.g. food preparers' hands).
- (iv) *Campylobacter* does not grow at ambient temperatures, survives well at refrigeration temperatures, and numbers are reduced by freezing (ICMSF, 1996).
- (v) High estimates of prevalence of contamination are associated with certain food products, such as fresh poultry, and the number of viable bacteria can vary very widely (several orders of magnitude) between individual food items from the same source, such as poultry carcasses from the same supplier.

3 MODELS: FEATURES AND IMPLICATIONS

3.1 Models and data

Before making a major decision, one first needs to collate all relevant information. The process of its collection and interpretation can be very time-consuming. It includes developing an overview of the relevant issues, followed by collecting detailed data that will influence the process. Finally the information has to be analysed. Quantitative models are increasingly being used for this purpose. When set up well, they will provide a framework that can also be used in future when similar issues arise.

This modelling project was distinctive in the sense that it brought food safety and environmental modelling together. The organism under investigation was *Campylobacter* but the framework that was developed can equally be used for other pathogens.

An overall *Campylobacter* model covering the whole New Zealand environment and food systems is not possible with the presently-limited data. The team has instead produced a number of models that are linked in various ways. These models were a team effort. The skills of the group included food safety and environmental knowledge, mathematical and statistical modelling and computer programming. This type of food safety and environmental models inevitably use a number of assumptions. The users of these models should consequently have adequate skills to understand these issues.

Not surprisingly, the dearth of information in some areas was problematic; for example, there are few data for the degree of surface water contamination by *Campylobacter*, beyond that collected by the Freshwater Microbiological Research Programme carried out in 1998-2000 at 25 freshwater recreational and drinking-water abstraction sites (McBride *et al.* 2002, Till *et al.* 2008). At this stage this still appears to be the problem with most food safety and (particularly) environmental models. This however, should not be seen as a weakness only of this project. In fact it has highlighted the need to collect more information, not ‘just’ to populate the models, but rather to provide risk managers with information that they could use to make a better informed decisions. Part of the risk manager’s job is to make sound decisions even when data is lacking, but it is still preferable to identify the most pressing data needs and deal with those depending on the resources available.

3.2 Who could use the models?

The current models cannot be used by ‘just anybody’. They are to assist people in the decision-making process to address the question: What is likely to be the effect of various interventions or mitigations? A question is who (or, more realistically perhaps, which groups) are appropriate users of the models?—Preferably in conjunction with other information and in collaboration with the developers.

Currently various groups of people are required to make such decisions regarding whether or not certain interventions are required that affect the load of bacteria (*E. coli*) and protozoa (oocysts of *Cryptosporidium* spp.) in waterways, especially with

regard to drinking-water supplies. Such decisions cannot be made without local geographic knowledge, biological knowledge and hydrological knowledge. These agencies may not always have the appropriate experience to use the models confidently, as statistical and computing knowledge is required as well. Some of these groups may not have these skills 'in house'—it may be necessary to engage consultants for this purpose. That of course invokes a cost which will have to be balanced against the possibility of improved knowledge that would become available to inform the decision-making process.

The models will require information that may not always be readily available. We have addressed this issue by providing detailed information in the accompanying technical reports, after extensive examination of New Zealand and overseas literature. In doing so, we note that the literature is not always harmonious and is sometimes ambiguous, as is often the case in an emerging field of science. Also some model inputs are rather variable (e.g., *Campylobacter* shedding rate by cows, as discussed in Table 2 in Elliott & Harper 2011). It is an option for the user to explore the literature quoted and amend the default values of the model if other information is deemed to be more appropriate.

Some limitations of the models can easily be spelled out, and we have attempted to do so. However it is extremely difficult to spell out all. Some stem from the statistical approach taken or assumptions underlying the microbiological tests. It is therefore important for model users to understand the assumptions, the models' structure and data accuracy. This requires an in-depth understanding of the model.

The Toenepi catchment area has been used as an example for an environmental model, particularly because it has a significant *Campylobacter* dataset (Stott *et al.* 2011). Conclusions regarding this catchment cannot be generally extrapolated to other catchments, but the model is capable of re-calibration to these by changing appropriate inputs and parameters (e.g., percentage of farmed stock with direct access to streams). In general geographic information is to be filled out by the user, while other biological and environmental information (e.g., hydrology, soil information, microbial inactivation coefficients) are to be acquired from the literature. And because that model requires considerable information and time to set up, with a large number of parameters (the values of which are uncertain), a simplified catchment risk model was developed to overcome some of these limitations. This used Monte Carlo modelling techniques, which are rather less demanding of detailed knowledge of environmental microbial processes and their rates.

3.3 Types of models

We have used a number of deterministic and stochastic approaches in constructing models, described in detail in the accompanying reports. Dynamic simulation was used for catchment modelling and farm disease transmission. "Monte Carlo" risk models feature prominently in pathway attribution via exposure assessment and in the simplified catchment risk model. In the latter, key exposure and dose-response inputs have been described by statistical distributions from which many sets of random samples have been taken to build a risk profile covering many eventualities. The studies for source attribution based on strain typing have included a number of

statistical model-based approaches; of particular note are the "Hald" and "Island" models (Wilson *et al.* 2008), used for inferring source attribution and strain virulence.

The exposure model also serves to indicate the degree of environmental contamination by *Campylobacter*—regardless of any health effect—and the interventions that may be useful for its reduction.

3.3.1 *Is the model appropriate and worthy of our trust?*

In all cases we have taken a "destructive testing" approach to the development and use of the models we report. This consists of applying plausibility, coherence and consistency checks to their performance.¹¹ If any result produced by a model fails one of these criteria its construction and coding has been revisited to identify, and to seek to redress, the cause of the problem.¹² In applying the models to various potential interventions, as described in the accompanying technical reports, we have indicated appropriate levels of confidence.

3.4 ESR Models

The exposure and attribution models developed by ESR focus on pathways of exposure, in contrast to the models developed by Massey which concern sources of *Campylobacter*. Exposure from a source may occur via multiple pathways, as described in Table 1.

The models have been developed to identify the relative importance of potential transmission pathways for campylobacteriosis, recognised in studies both overseas and in New Zealand:

- Food consumption (chicken, beef, sheep meat, pork, offal, duck and turkey meat)
- Drinking water consumption
- Recreational water use
- Exposures associated with young children (0-4 years) living in a rural environment (potentially including drinking water, so this population is excluded from drinking water consumption modelling to avoid double counting)
- Overseas travel
- Occupations (that involve working with potentially contaminated animals or sick people)
- Pets and other animal contact
- General contact between uninfected and sick people

These models generate outputs that attribute fractions of the overall campylobacteriosis burden as represented by the number of notified cases in a year.

The number of *Campylobacter* cells ingested by humans, i.e., exposure, might be estimated for the first three pathways listed and this approach was intended to be used in models to estimate the relative importance of these pathways. Although an

¹¹ This is inherent in the "Bradford-Hill" criteria when addressing issues of association versus causation in the medical sciences (Hill 1965).

¹² This practice follows the wise (paraphrased) dictum attributed to the influential statistical Dr George E. Box: "All models are wrong, some are useful".

exposure model for drinking water was constructed after review of the available data, it was decided that suitable input parameters could not be derived. Consequently only exposure estimate models for food and recreational water were used to generate pathway attribution.

There are insufficient data to estimate exposures for the other five pathways, so the proportion of campylobacteriosis cases attributed to these pathways must be estimated indirectly. This was achieved by analysing data from notified cases of campylobacteriosis in New Zealand, alongside analyses of notified cases and sources of *Campylobacter* from a sentinel site in the Manawatu.

Table 1: Sources and pathways for human *Campylobacter* attribution modelling

		PATHWAY							
		Food Eating / Preparation	Drinking Water	Recreational Water	Rural Pre- school children	Occupation	Animal Contact	Faecal Contact	Overseas Travel
SOURCE	Pets			X		X	X	X	
	Poultry	X			X	X	X	X	
	Cows/Sheep/Pigs	X	X	X	X	X	X	X	
	Wild Animals / Birds		X	X	X			X	
	Environmental / Water		X	X	X	X		X	
	Human	X	X	X		X		X	
	Overseas								X

Four models have been developed by ESR:

3.4.1 Comparative Exposure Model for Food

This model (the “Food Model”) predicts the number of human infections based on exposures to *Campylobacter* from consumption of chicken, beef, sheep meat, pork, offal, turkeys and ducks.

3.4.2 *Comparative Exposure Model for Drinking Water*

This model (the “Drinking Water Model”) predicts the number of human infections based on exposures to *Campylobacter* from consumption of drinking water.

3.4.3 *Comparative Exposure Model for Recreational Water*

This model (the “Recreational Water Model”) predicts the number of human infections based on exposures to *Campylobacter* from consumption of surface water through recreational swimming in the natural environment.

3.4.4 *Pathway Attribution Model*

This model (the “Pathway Model”) brings together attribution based on (i) analyses of notified campylobacteriosis cases (ii) attribution based on strain types identified in a sentinel study in the Manawatu, and (iii) the number of human infections predicted by the food and recreational water exposure models.

3.4.5 *Synthesis of ESR model findings*

Figure 1 presents the model estimates for the relative attribution of notified campylobacteriosis cases for New Zealand in 2006 and 2008 to each transmission pathway. Analysis of these two years was conducted because in 2007 interventions were put into place by the poultry industry to reduce *Campylobacter* in retail poultry alongside the introduction of a regulatory *Campylobacter* Performance Target by the NZFSA. This is considered to have reduced the incidence of notified campylobacteriosis in New Zealand (Sears *et al.* 2011).

The intervals on the attribution estimates are plausible intervals representing the lower and upper bounds of the attribution estimate based on analysis of the different data sources and are discussed in detail in Lake *et al.* (2011). The different data sources mean that different approaches have been used to generate the bounds: The bounds for the risk factor analyses (occupational exposure, rural 0–4 year olds, overseas travel and person to person transmission) are from direct observation of the notification data. The bounds for the cat and dog pathways are generated using interval analysis incorporating the 95th credible interval from source attribution analysis. The bounds for the exposure models (food and recreational water) are generated using interval analysis incorporating bounds on the size of exposed population and the 2.5th and 97.5th percentiles of the Monte Carlo simulations.

It is important to note the attribution estimate for the unassigned notifications (including drinking water and other animal contact) has been generated by difference. Plausible bounds for the number of unassigned notifications have not been calculated and are not given in the Figure.

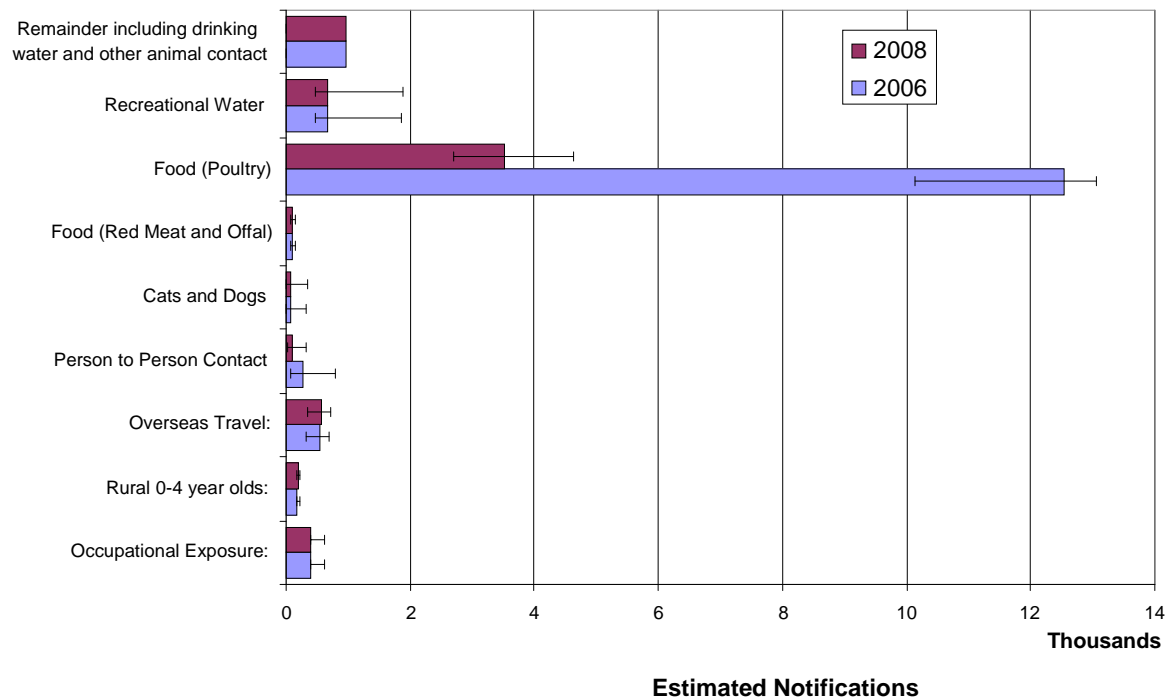


Figure 1 Estimated relative attribution of notified campylobacteriosis cases for New Zealand in 2006 and 2008. Plausible interval not plotted for ‘remainder’ pathway.

The analysis generated from the ESR models represents an alternative approach to understanding the transmission of campylobacteriosis in New Zealand. This topic has to date been investigated by case-control studies (Eberhart-Phillips *et al.* 1997, Ikram *et al.* 1994) and source attribution using strain typing (Mullner *et al.* 2009, Mullner *et al.* 2010a), as well as analysis of notification and hospitalisation data (Baker *et al.* 2007).

The notification data used to attribute the relative importance of pathways involves (i) geographical location of the cases (for urban/rural analyses), (ii) occupation, and (iii) overseas travel preceding notification (and hence the likelihood that the infection was acquired overseas).

Risk factor data for notifications are incomplete and potentially subject to selection bias amongst those who are notified from the totality of community cases, and bias in reporting of the data on these cases by public health sources. To compensate for this, notification data were reviewed by region, and only data from regions where more than half the notified cases reported the relevant data were used to estimate a rate of notification for the three population groups (overseas travellers, young children in rural environments, various occupational groups). This rate was used to calculate a corrected proportion of notifications, by multiplying the rate by national data (from Statistics New Zealand sources), on the size of the three populations. Nevertheless, there remains the potential for bias in the notification data e.g., occupations at higher risk of infection may be more likely to be reported during the notification process than others.

Some of the estimates in this analysis can be compared with other studies. The exposure assessment approach for exposures to *Campylobacter* in chicken for 2008 is broadly in agreement with the source attribution analyses using strain typing for the Manawatu region which show that poultry is an important source (approximately 25% of cases attributed to poultry associated types in 2008) (French *et al.* 2011, Sears *et al.* 2011).

The source attribution analyses have also found that cases in rural areas were more likely to be infected with ruminant associated types than urban areas (Mullner *et al.* 2010b). More than half of the cases in the Manawatu have been attributed to ruminant (cattle, sheep) associated types in 2008 (French *et al.* 2011). Given the apparently low prevalence of contamination of ruminant derived foods (beef and sheep meat) at retail (French 2008, Wong *et al.* 2007), and low consumption of more frequently contaminated ruminant derived foods (offal) (Cressey *et al.* 2006), there is a question about the transmission routes for these types. Transmission pathways involving animal contact and contaminated water are plausible routes for such exposures, and this analysis has highlighted the potential importance of these factors.

3.5 Massey University models

The resources allocated to Massey University in this project have been used to generate new data on *Campylobacter* typing and for construction of two models:

- “New and emerging data on typing of *Campylobacter* spp. strains in animals, environmental matrices and humans”—to isolate and type *Campylobacter* from a number of sources to augment the archive of isolates at the Hopkirk Research Institute, and improve the data available for source attribution modelling;
- “Modelling of *Campylobacter* carriage and transmission between and within animal groups.”

Two sets of models have been produced. They are presented here with a synthesis of their main findings.

3.5.1 Genotype Source Attribution Models

New studies on *Campylobacter* spp. isolated from different matrices have provided over 4,000 *C. jejuni* and *C. coli* isolates from over 10,500 samples tested from humans, poultry, red meat and offal, environmental water, and faecal material from domestic and wild animals. Details of the sampling rationale are given in the accompanying technical report (French *et al.* 2011). A total of 2666 isolates yielded full multilocus sequence typing (MLST) allelic profiles and these have been used to update source attribution models. These models were used to estimate both the source of human infections, and the source of *C. jejuni* in environmental water.

Using the additional genotyping information provided by this study, the major source of isolates recovered from water was estimated to be water birds (between 40% and 70% depending on the choice of model.) This followed the discovery that water birds were carriers of the most common Sequence Type recovered from surface water. Some of the strains recovered from wild birds have been identified in human clinical cases, but most have only been isolated in water and wild birds, and they are therefore

assigned a low 'virulence' score in relative exposure models. The next most important source of *C. jejuni* in water was estimated to be sheep (>10%).

The extended and updated source attribution models for human cases in the Manawatu still consistently identify poultry as the most common source of human infection; although dynamic attribution modelling has shown a marked reduction in poultry-associated cases following the introduction of the *Campylobacter* in poultry risk management strategy. In contrast recreational water was assigned a very low contribution to human cases, largely due to the dominance of water-bird associated Sequence Types in water samples, and evidence that these were rarely found in human clinical cases. However, many of the human cases that were attributed directly to cattle and sheep could have been infected via non-food exposures such as untreated drinking water, and this could explain the prominence of these strains in rural areas, and the relatively high notification rate in rural pre-school children. The work on relative virulence outlined in French *et al.* (2011) indicates that most of the water-associated genotypes are possibly of low infectivity, with the exception of those attributable to ruminants. However, only recreational water sites were sampled, so attribution estimates don't truly reflect all water-related exposures. It is therefore possible that many of the cases currently assigned to ruminants in source attribution models are attributable to untreated drinking supplies in rural areas. These could represent drinking water contaminated locally from the (small) upstream contributing area.

Source attribution modelling indicated only a small proportion (<3%) of human cases were directly attributable to wild bird sources. Less than 5% of samples from dogs and cats were positive for *C. jejuni*, but most of the Sequence Types recovered were associated with human infection. There was some discrepancy between models, but both the Hald and Island models estimated a very small contribution from cats and dogs to the burden of human cases (<2%). The extended sampling of water birds in this study recovered key water-associated Sequence Types from water birds, for example the most common Type in water in New Zealand (ST 2381) was isolated from Pukeko—this strain has not been found in human isolates.

3.5.2 Carriage and Transmission Model

This model incorporates pathogen carriage and transmission between and within animal groups. It uses multi-group transmission models to capture the non-linear stochastic dynamics of infection in populations of animals and the environmental cycling of pathogens. It has been developed for transmission on a typical New Zealand dairy farm, including seasonal calving and the resulting lactating and dry cycles in adult animals. Also, given the evidence of small subgroups of animals being responsible for the majority of pathogen transfer ("high-shedders", Marshall & French 2010), differential shedding of animals within each management group is incorporated. Two specific interventions are assessed: (i) Isolating of a particular group of animals to limit between-group transmission, (ii) Targeted active intervention on the "high-shedder" animals. The first highlights the seasonal linkages between groups and how isolating a single management group may have carry-on effects that reduce the prevalence in all groups. The second shows that targeting "high-shedder" animals can be effective at reducing overall prevalence and environmental loading significantly even when only modest reductions in numbers of animals shedding are achieved. An extension of the model into a catchment framework is demonstrated, showing how the

stream network may be viewed as a pathway for between-farm transmission of pathogens.

3.6 NIWA models

Two models have been produced. They are presented herein with a summary of their main findings.

3.6.1 *Detailed Catchment Deterministic Model*

This model represents the deposition of animal wastes from a range of animal types on the ground and directly into streams, as well as wash-off from the land during storm conditions. These processes are examined in considerable temporal (hourly or sub-hourly) and spatial detail. A dynamic stream routing model is included. This has been applied to and calibrated for the dairy-dominated Waikato Toenepi catchment—which has the most abundant datasets for *Campylobacter* (and *E. coli*).

The model provides a reasonable representation of the flow, and exhibits a moderate performance for concentrations. It is sensitive to a number of uncertain parameters, and it would be difficult to calibrate fully. The model does, however, provide a plausible representation of key processes and responses. For example, the shedding rate and stock numbers were found to affect loads and concentrations strongly. Parameters associated with washoff of faecal material affected loads and storm concentrations, but had little effect on baseflow concentrations. Stock access to streams had a strong effect on baseflow concentrations but not on storm-flow concentrations. Dairy effluent disposal had a small or moderate effect on baseflow concentrations. Wildfowl have the potential to significantly increase concentrations (of thermotolerant *Campylobacter*) during baseflow. This model is available as a Microsoft Visual Basic file with data inputs via Excel spreadsheets.

3.6.2 *Catchment Risk Model*

This model provides an opportunity for rapid assessment of various catchment loadings of *Campylobacter* and the associated water quality response. It captures many of the key processes and microbial sources in the dynamic model uses a simplified representation of the processes and a coarser temporal and spatial resolution, but includes consideration of parameter variation and uncertainty through a Monte Carlo simulation. It is implemented via the use of the @Risk Excel plug-in. Both models include consideration of dairy waste disposal, and the risk model includes simple components for chicken litter application and human waste (using a synthesis prepared for this project, Elliott 2011). The model has been applied to some large catchments (from the Freshwater Microbiological Programme's dataset, Till *et al.* 2008), and has been used to help assess the implications of a range of intervention measures in related phases of the overall research programme (as described in Elliott & Harper 2011).

The following two separate analyses have also been developed through the project and have helped to construct the two NIWA models.

3.6.3 *Modified Dose-Response Model*

In this analysis (McBride & French 2011) a SIR model¹³ for *Campylobacter* infections was used to modify the values of the standard "beta-Poisson" dose-response curve parameters (α and β , reflecting infectiousness—Teunis & Havelaar 2000). This modified response is for *Campylobacter* infection among healthy rural adults: the β parameter was raised to a value of 50, to reflect that group's inferred higher immunity status, attributable to more regular exposure to the pathogen. This work also noted that available data indicates that children face much higher risks of infection *and* disease, given exposure to *Campylobacter* (from consumption of unpasteurised milk during farm visits, Teunis *et al.* 2005) such that the beta-Poisson model could be replaced by a simple exponential model with a rather lower median infectious dose).

3.6.4 *Multi-farm Analytical Model*

The potential for transmission between farms via stream supply of animal drinking water is examined using a simplified mathematical approach (McBride & Chapra 2011). This model highlights the potential amplification of carriage via feedbacks between stock emissions to streams and infection from stock water derived from streams. While new results from a DairyNZ-funded study for the Toenepi farms indicate that transmission between-farms is more likely between adjacent farms than via stream water (French *et al.* 2010) it is notable that this model and the Carriage and Transmission model both predict the possibility of farms becoming sterile for *Campylobacter* under stringent conditions, such as isolation of infective animals and targeted active intervention on the small proportion of "high shedder" animals.

¹³ SIR denotes the Susceptible-Infected-Recovered class of models (Anderson & May 1991).

4 LINKING THE MODELS TO ASSESS INTERVENTIONS

4.1 How does one inform the other?

An inherent value of a collaborative project such as this one is the pooling of knowledge and collaborative approaches taken to addressing the problem. More formally, the development of models by each individual science provider has informed and contributed to model development by the others. Specifically:

- Dose-response alternate parameter settings for people with (partial) immunity: models developed by NIWA-Massey have been used in the exposure assessment models developed by ESR.
- Source attribution findings for person to person and pets from MLST and notification data from the Manawatu modelled by Massey University have been used in the pathways model developed by ESR.
- Aggregate differential infectivity factors for types of *Campylobacter* found in sources compared to those in human cases from the Manawatu by University have been used in the exposure assessment models developed by ESR.
- Reductions in animal shedding for different farm management practices predicted by the Carriage and Transmission Model have been used as input to the Catchment Risk Model. The latter model also received guidance for other mitigations (e.g., fencing stream banks) from the Dynamic Catchment Model.

4.2 Using the models to investigate interventions

The accompanying technical reports contain examples of how the models have been used to explore a range of potential interventions, aimed at reducing the amount of environmental contamination and the associated burden of campylobacteriosis. These include the manner in which models were linked. We suggest that these examples do indicate that some potential interventions are highly likely to have a beneficial effect. For example, fencing streams in cattle farming areas would significantly lower *Campylobacter* concentrations in streams—were full fencing to be implanted in a catchment with minimal fencing—concentrations would be reduced by more 50%.

5 CONCLUSIONS

A number of models have been developed aimed at acquiring a better understanding of the ecology of *Campylobacter* in the environment, as well as attribution to sources and pathways of infection for people. In considering these matters we recommend that the following findings should be borne in mind.

1. The source attribution and pathway models have shown that while the poultry component has declined (given the interventions already undertaken), poultry is still a significant part of the overall attribution and so further risk management may prove beneficial in terms of burden reduction
2. Human campylobacteriosis cases in the Manawatu attributed to cattle and sheep in 2008 exceeded those attributed to poultry. These findings were obtained using two different models which were informed by strain-typing funded in part funded by this project.
3. The pathway model has shown that the individual contributions of a number of other risk factors to the total predicted disease burden are relatively small. These have been categorised as: occupational exposure, exposures for 0-4 year olds living in a rural environment, overseas travel, person-to-person contact, contact with cats and dogs, red meat and offal, and recreational water exposure.
4. Based on data from notified cases, there is a higher risk of illness amongst 0-4 year olds living in a rural environment, compared to those children living in urban environments.
5. The pathway modelling has identified a “remainder” proportion of the attribution that cannot currently be assigned. This remainder will include a variety of exposures, including those from drinking water, as well as “other” animal contact (i.e., excluding animal contact already addressed by the model), and consumption of other foods such as unpasteurised milk.
6. The exploration of available data (by this project) to populate an exposure model for drinking water has revealed a shortage of information on key inputs, particularly:
 - Populations served by unregistered water supplies
 - Water sources and treatment status of such unregistered supplies
 - Frequency of exposure to drinking water outside of the normal home supply (e.g. exposures for urban populations during camping trips, farm visits etc.)
7. The environmental models, aided by further strain typing of isolates from river water during flood flows (funded by DairyNZ), confirm that *Campylobacter* concentrations during low flow periods are usually low and are dominated by wild bird species. However during flood periods concentrations become much higher, are dominated by ruminant species, and this is the result of local runoff from farmed areas.
8. Information is lacking on the relative importance of surface washoff of *Campylobacter* versus infiltration flow contaminant pathways from faecal deposits on the land to waterways (identified in the findings of the earlier CDRP-funded project "Pathogen Transmission Routes Research Programme").

6 REFERENCES

* Denotes publications prepared explicitly for this project

- Anderson RM and May R (1991). *Infectious Diseases of Humans*. Oxford, UK.
- Alexander RB and McBride GB (2011, in prep.) Explaining occurrence of zoonotic pathogens and their indicators in multiple watersheds. For submission to *Nature*.
- Baker MG, Sneyd E and Wilson NA (2007). Is the major increase in notified campylobacteriosis in New Zealand real? *Epidemiology and Infection* **135**: 163–170.
- Close M, Noonan M, Hector R and Bright J (2010). Microbial Transport from Dairying under Two Spray-Irrigation Systems in Canterbury, New Zealand. *Journal of Environmental Quality* **39**: 824–833.
- Collins R, McLeod M, Hedley M, Horne D, Hanly J, Close M, Bagshaw C, Donnison A, Ross C and Matthews L (2005). Pathogen transmission routes: Farm animals to waterways – Best Management Practices. Client Report HAM2005-071. A report for the Ministry of Agriculture and Forestry, National Institute of Water and Atmospheric Research (NIWA), Hamilton, June.
- Collins R, McLeod M, Hedley M, Donnison A, Close M, Hanly J, Horne D, Ross C, Davies-Colley R, Bagshaw C and Matthews L (2007) Best management practices to mitigate faecal contamination by livestock of New Zealand waters. *New Zealand Journal of Agricultural Research* **50**: 267–278.
- Cressey P, King N and Lake R (2006) Food consumption data for risk assessments. Client Report FW0602. A report for the New Zealand Food Safety Authority. ESR: Christchurch Science Centre.
- Eberhart-Phillips J, Walker N, Garrett N, Bell D, Sinclair D, Rainger W and Bates M (1997). Campylobacteriosis in New Zealand: results of a case control study. *Journal of Epidemiology and Community Health* **51**: 686–691.
- *Elliott S (2011). Preliminary risk model for environmental losses of *Campylobacter* from broiler litter. Client Report HAM2010-062. Prepared for the New Zealand Food Safety Authority and Ministry for the Environment, National Institute of Water and Atmospheric Research (NIWA), Hamilton.
- *Elliott S and Harper S (2011). Catchment models for *Campylobacter*: Detailed Dynamic Model and Associated Risk Model. Client Report HAM2010-069. A report for the New Zealand Food Safety Authority and Ministry for the Environment, National Institute of Water and Atmospheric Research (NIWA), Hamilton and Auckland.
- French N (2008) Enhancing surveillance of potentially foodborne enteric diseases in New Zealand: Human campylobacteriosis in the Manawatu. Hopkirk Institute, Massey University, NZ.
- French N. and Marshall J (2010). Report: NZFSA Agreement 11777, Schedule 1A Source attribution July 2009 to June 2010 of human *Campylobacter jejuni* cases from the Manawatu. Molecular Epidemiology and Public Health Laboratory, Massey University, Palmerston North. Prepared for the New Zealand Food Safety Authority, December.
- French N, Donnison A, McBride G, Irshad H and Sukias J (2010). Final Report to DairyNZ for Schedule Number BS808 on the topic "Transmission of two zoonotic pathogens". NIWA, AgResearch, Massey University, June.

- *French NP, Marshall J and Mohan V (2011). *Campylobacter* in food and the environment: new and emerging data on typing of *Campylobacter* strains in animals, environmental matrices and humans. Final report 07-10436, Molecular Epidemiology and Public Health Laboratory, Massey University, Palmerston North. Prepared for the New Zealand Food Safety Authority and Ministry for the Environment.
- Hill AB (1965). The environment and disease: association or causation? *Proceedings of the Royal Society of Medicine* **58**: 295–300.
- ICMSF (1996). *Campylobacter*. In: “Microorganisms in Foods 5”. In: Microbiological Specifications of Food Pathogens, pp. 45–65. International Commission on Microbiological Specifications for Foods. Blackie Academic and Professional, London.
- Ikram R, Chambers S, Mitchell P, Brieseman MA and Ikram OH (1994). A case-control study to determine risk-factors for *Campylobacter* infection in Christchurch in the summer of 1992-3. *New Zealand Medical Journal* **107**: 430–432.
- Lake R, Adlam B, Perera S, Campbell DM and Baker MG (2010). The disease pyramid for acute gastrointestinal illness in New Zealand. *Epidemiology and Infection* **138**(10): 1468–1471.
- *Lake R, Horn B and Ball A (2011). *Campylobacter* in food and the environment: examining the link with public health. Pathway attribution. Client Report FW10007. A report for the New Zealand Food Safety Authority and Ministry for the Environment. ESR: Christchurch Science Centre.
- *McBride GB (2011). Explaining differential sources of zoonotic pathogens in intensively-farmed catchments using kinematic waves. *Water Science and Technology* **63**(4): 695–703.
- McBride G, Till D, Ryan T, Ball A, Lewis G, Palmer S and Weinstein P (2002). Freshwater Microbiology Research Programme Report: Pathogen Occurrence and Human Health Risk Assessment Analysis. Ministry for the Environment and Ministry of Health, Wellington.¹⁴
- McBride G, French N, Donnison A, Nagels J and Ross C (2009). Progress Report to DairyNZ for Schedule Number BS808 on the topic "Transmission of two zoonotic pathogens". NIWA, AgResearch, Massey University, May.
- *McBride, GB and French NP (2010, in prep.) Modifying the campylobacteriosis beta-Poisson dose-response model to account for differential immunity between groups. For submission to *Epidemiology and Infection*.
- *McBride G and Chapra C (2011). New hydroepidemiological models of indicator organisms and zoonotic pathogens in agricultural watersheds. *Ecological Modelling*. doi 10.1016/j.ecolmodel.2011.04.008.
- *Marshall J and French N (2010). Modelling *Campylobacter* carriage and transmission between and within animal groups. Final report: 07-10436, Molecular Epidemiology and Public Health Laboratory prepared for the New Zealand Food Safety Authority and Ministry for the Environment.
- MfE/MoH (2003). Microbiological water quality guidelines for marine and freshwater recreational areas. Published by the Ministry for the Environment for the Ministry for the Environment and the Ministry of Health, Wellington.¹⁵

¹⁴ <http://www.mfe.govt.nz/publications/water/freshwater-microbiology-nov02/>

¹⁵ <http://www.mfe.govt.nz/publications/water/microbiological-quality-jun03/>

- Mullner P, Jones G, Noble A, Spencer SE, Hathaway S and French NP (2009). Source attribution of food-borne zoonoses in New Zealand: a modified Hald model. *Risk Analysis* **29**: 970–984.
- Mullner P, Collins-Emerson JM, Midwinter AC, Carter P, Spencer SE, van der Logt P, Hathaway S and French NP (2010a). Molecular epidemiology of *Campylobacter jejuni* in a geographically isolated country with a uniquely structured poultry industry. *Applied Environmental Microbiology* **76**: 2145–2154.
- Mullner P, Shadbolt T, Collins-Emerson JM, Midwinter AC, Spencer SE, Marshall J, Carter PE, Campbell DM, Wilson DJ, Hathaway S, Pirie R and French NP (2010b). Molecular and spatial epidemiology of human campylobacteriosis: source association and genotype-related risk factors. *Epidemiology and Infection* **138**(10): 1372–1383.
- Sears A, Baker M, Wilson N, Marshall J, Mullner P, Campbell D, Lake R and French N (2011). Marked national decline in campylobacteriosis following interventions aimed at poultry. *Emerging Infectious Diseases*. In press.
- Stott R, Davies-Colley R, Nagels J, Donnison A, Ross R and Muirhead R (2011). Differential behaviour of *Escherichia coli* and *Campylobacter* spp. in a stream draining dairy pasture *Journal of Water and Health* **9**(1): 59–69.
- Teunis PFM and Havelaar AH (2000). The beta-Poisson dose-response model is not a single-hit model. *Risk Analysis* **20**(4): 513–520.
- Teunis P, van den Brandhof W, Nauta M, Wagenaar J, van den Kerkhof H and van Pelt W. (2005). A reconsideration of the *Campylobacter* dose-response relation. *Epidemiology and Infection* **133**: 583–592.
- Till DG and McBride GB (2004). Potential public health risk of *Campylobacter* and other zoonotic waterborne infections in New Zealand. Chapter 12 In: Cotruvo JA *et al.* *Waterborne Zoonoses: Identification, Causes and Control*, IWA publishing, London, for the World Health Organization.¹⁶
- Till D, McBride G, Ball A, Taylor K and Pyle E (2008). Large-scale microbiological study: Rationale, results and risks. *Journal of Water and Health* **6**(4): 443–460.
- WHO/FAO (1959). *Second Report of the Joint WHO/FAO Expert Committee on Zoonoses*. WHO Technical Report Series No. 169, World Health Organization, Geneva.
- Wilson DJ, Gabriel E, Leatherbarrow AJH, Cheesbrough J, Gee S, Bolton E, Fox A, Fearnhead P, Hart CA and Diggle PJ (2008). Tracing the Source of Campylobacteriosis. *PLoS Genetics* **4**(9): e1000203.
- Wong TL, Hollis L, A, Nicol C, Cook RC and Hudson JA (2007). Prevalence, numbers, and subtypes of *Campylobacter jejuni* and *Campylobacter coli* in uncooked retail meat samples. *Journal of Food Protection* **70**: 566–573.

¹⁶ http://www.who.int/water_sanitation_health/diseases/zoonosessect4.pdf

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