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Preliminary Relative Risk Assessment for *Campylobacter* Exposure in New Zealand:

1. National Model for Four Potential Human Exposure Routes
2. Farm Environmental Model

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Preliminary Relative Risk Assessment for *Campylobacter* Exposure in New Zealand:

1. National Model for Four Potential Human Exposure Routes

2. Farm Environmental Model

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Prepared for

Ministry of Health and Enteric Zoonotic Disease Research Group Steering Committee

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Executive Summary

The high reported rates of campylobacterosis in New Zealand over the past two decades has prompted several investigations into the sources, transmission routes, and exposures of humans to *Campylobacter*. Previous work in New Zealand and in other countries has suggested that food, particularly undercooked poultry and cross-contamination with other foods within the kitchen during the storage and preparation of poultry, is the single most important exposure. However, numerous other exposures have been identified such as drinking water, recreational swimming, and contact with livestock, which may also be important.

Key previous studies on campylobacterosis in New Zealand include the case-control "MAGIC" study, published in 1997, which has shed considerable light on these issues. The **Campy1 Model** was developed in 2000 to examine the complex network of pathways and identified numerous gaps in our knowledge. The 2002 **Water_Simple Model** was developed to explore the flow of *Campylobacter* through the freshwater environment. It found that a high proportion of *Campylobacter* in streams was from dairy cattle and sheep.

The work presented in this report builds on these previous efforts. It arose when the Modelling Group of the Enteric Zoonotic Diseases Research Group was commissioned to explore *Campylobacter* routes, transmissions and exposures through a holistic modelling approach. To accomplish this goal, we built the following two models, one of which explores the relative importance of four of the most commonly identified infection exposures and the other which explores the persistence of *Campylobacter* in a rural setting.

***Campylobacter* Human Exposure Model.** Whereas the **Campy1 Model** considered all known pathways (i.e., sources, routes and exposures) between humans, animals, and the environment, the purpose of this model was to focus on the relative importance of four potentially important exposures to *Campylobacter* infection: food (poultry and red meat, including cross contamination); drinking water (three grades of good, poor, and untreated); freshwater swimming; and occupational contact (livestock). We have tentatively concluded that of these, cross-contamination during preparation or storage of poultry, and to a lesser extent red meat, were the most important exposures. The least important was drinking well-treated water. Occupational contact with livestock was also identified as important, though very little information exists to verify this result. The MAGIC study did not identify "Occupational contact with cattle" as a significant risk factor. However it was essentially an urban study (only 14.3% of case-patients were from a rural area). The relative risk of infection from the remaining exposures was low compared to cross-contamination from poultry during storage or food preparation. Note that this is all based on dose-response data for *Campylobacter jejuni*: there are no data for other *Campylobacter*. Sensitivity studies show that the input parameters to which the model was most sensitive were the probabilities that poultry or red meat were contaminated.

***Campylobacter* Farm Environmental Model**. The **Water_Simple Model** predicted the movement of *Campylobacter* through New Zealand's aquatic environments and found that the dairy farm is a relatively important source of these micro organisms. The ***Campylobacter* Farm Environmental Model**, which is an extension of the **Water_Simple Model**, predicts the movement of *Campylobacter* through a hypothetical farm (which includes the cows, dairy shed, paddock, and stream). Within this framework, we are able to explore the persistence of *Campylobacter* in the environment and simulate the relative performance of various management practices and intervention measures. Though this model is in the early stages of development, initial results suggest that animals permitted to defecate in the stream may increase the *Campylobacter* levels within the stream to levels capable of infecting downstream animals.

Information gaps

During the development of the models described within this report, several areas of data or knowledge deficiency have been identified. The identification of such areas using a structured modelling methodology is a valuable tool for the effective and efficient targeting of future research. Furthermore, this research may be prioritised by identifying which of these data deficient variables has the most influence on the model output.

The following knowledge gaps were found while making these models:

- Factors involved in occupational exposure (the ***Campylobacter* Human Exposure Model** is somewhat sensitive to variables associated with this factor; more importantly, we have less secure means of modelling this exposure pathway).
- Human dose-response, especially the chance of infection at low doses, and the dose-response for multiple strains of *Campylobacter* and for *Campylobacter* species other than *C. jejuni.*
- Animal dose-response (the ***Campylobacter* Farm Environmental Model** needs better data on this aspect).
- Immunity from repeat exposures, especially by farm workers.
- Better data on the numbers of *Campylobacter* on red meat.
- Prevalence and concentration of *Campylobacter* in farm animals.

Accordingly, we cannot say that this model has been validated, so its results should be interpreted with some caution.

1. Introduction

The background to this project is the New Zealand Government's interest in significantly reducing New Zealand's high reported rate of campylobacterosis. This illness contributes the majority of the economic burden of gastrointestinal disease in this country (Scott et al. 2000).[1]

To assist in this endeavour, the Enteric Zoonotic Disease Research Steering Committee set up a Modelling Group to identify and collate all data (both published and unpublished) relevant to New Zealand and to initiate development of quantitative risk assessment (QRA) models to help elucidate sources, routes and exposures of *Campylobacter*. This group comprises staff of NIWA, ESR and NZFSA. The modelling exercise, funded by the Ministry of Health and latterly by the Poultry Industry Association of New Zealand, has been carried out primarily by NIWA staff, reporting back to three separate meetings of the Modelling Group in the period late May to early September 2004, and in subsequent correspondence. Hence, while this is strictly a NIWA client report, it includes the other members as authors and their organisations logos. The findings reported here represent a consensus of the group.

In developing the models we have made use of previous New Zealand research as antecedents, in particular:

MAGIC A multi-centre case-control epidemiological study carried out in the mid 1994–95 (Eberhardt-Phillips et al. 1997).

Campy1 An elaborate dynamic differential equation model coded in a simulation language (ACSL) (Zwart and McBride 2000).

Water_Simple A QRA model aimed at explaining the relative contributions of various *Campylobacter* sources to the amount found in natural waters (Skelly 2002).

In particular, **Campy1** has demonstrated a number of knowledge gaps, and while being useful as a research tool, is not appropriate for management decision-making. **Water_Simple** has indicated that cattle may be the major contributor to the amount of

[1] The current reported campylobacteriosis rate in New Zealand is 2 to 10 times greater than rates reported in other developed countries (e.g., Australia, Austria, Belgium, Denmark, England and Wales, Finland, Germany, Greece, Iceland, Ireland, Northern Ireland, Norway, Scotland, Spain, Sweden, Switzerland, The Netherlands, and The "FoodNet" estimates from the United States—Reiersen et al. 2001, Spencer 2004). While there are issues in deciding whether these differences are attributable to different surveillance and reporting systems, it is generally agreed that the rate of campylobacteriosis in New Zealand has risen in recent years (although it fell by approximately 17% from 2003 to 2004).

Campylobacter found in environmental water.[2] The MAGIC study reported that factors associated with chicken consumption (e.g., consumption of "raw or undercooked" chicken, chicken consumed away from home), were the major risk factors for human infection, with lesser contributions from unpasteurised milk, consumption of raw or undercooked meat or fish, and puppy ownership. Amongst the other risk factors identified were: overseas travel, rainwater as a source of home water supply, sewerage problems, handling calf or bovine faeces, pets with diarrhoea, contact with cattle or calves (although solely occupational contact with cattle or calves did not achieve statistical significance) and occupational contact with cattle and calf carcasses.

In addition to these antecedent projects, this modelling exercise took account of a number of other applicable QRAs developed both in New Zealand (e.g., *Salmonella* Brandenburg in sheep meat, and *Campylobacter* in poultry meat) and overseas.

With this background we have approached the task before us by developing two models, each addressing different questions:

An exposure model	From where do infected humans ingest these pathogens?
An environment model	How did the pathogens get to the point of exposure, and where did they come from? (So far this has focussed on a hypothetical farm.)

The first model, the ***Campylobacter* Human Exposure Model**, estimates the relative importance of four commonly identified exposures to *Campylobacter* in New Zealand: recreational swimming, drinking water, food (poultry and red meat), and occupational animal contact. It presently ignores other foods (particularly unpasteurised milk and offal) and contact with pets. The focus is on domestic exposures that are more amenable to risk management; overseas travel is an acknowledged risk factor but has also not been included in the model. Person-to-person transmission of *Campylobacter* infection is infrequent compared to other bacterial infections.

The second model, the ***Campylobacter* Farm Environmental Model**, simulates the movement of *Campylobacter* through a hypothetical dairy farm to a stream. The key feature of this model is the feedback between the deposition of *Campylobacter* into the environment by the cows and the ingestion of *Campylobacter* by the cows from the environment. It should be noted that in no way does our presentation of this model

[2] We note that **Water_Simple** doesn't include landscape features, so the increased runoff from hillslopes where sheep predominate is not included. The Freshwater Microbiological Research Programme's results show that dairy-dominated catchments had similar levels of *Campylobacter* contamination in their water as did sheep dominated catchments (McBride et al. 2002). **Water_Simple** also does not include the fate of poultry faecal material, much of which is spread onto pasture.

in this report suggest that dairying represents any greater risk than the other identified transmission routes. For example (as noted already in footnote 2), results in the Freshwater Microbiological Research Programme showed that catchments dominated by dairy farming had similar *Campylobacter* concentrations to those in sheep farming (McBride et al. 2002). Furthermore, runoff from steeper sheep-grazing lands can contain high levels of faecal contamination, even when vegetated buffer strips are used (Collins et al. 2005).

In the time scale for this project these models are necessarily rather generalised, addressing order-of-magnitude issues. Yet, this two-model approach has proved to be fruitful. What follows is a brief description of the two models, followed by a discussion of the results. Some important features of this developmental modelling exercise should be noted. In the words of an eminent statistician "Models, of course, are never true, but fortunately it is only necessary that they be useful." (Box 1976). The models' usefulness depend heavily on the validity of their underlying assumptions, and while we have sought to use all available New Zealand data known to us, these models have yet to be fully tested.

2. Model Descriptions

2.1 *Campylobacter* Human Exposure Model

During a two-day workshop (May 25 and 26, 2004), we developed a QRA model for *Campylobacter* exposure in @Risk 4.5 (Palisade Corp., 2003), which is an add-in program for Microsoft's EXCEL, providing a development platform for risk assessment models. The purpose of this model is to explore the relative risk of *Campylobacter* infection by exposure to four sources of *Campylobacter*: food (poultry and red meat); freshwater swimming, three grades of drinking water (good, poor, and untreated); and occupational exposure (livestock). The model uses a Monte Carlo approach to determine whether a hypothetical New Zealander might be exposed and then infected, based on the probability of *Campylobacter* exposure through the four exposure pathways on a given day (Figure 1). For each iteration day, the dose from each of the four pathways is summed to obtain the total dose for this iteration (which represents an average individual on an average day). Also, on each of those days a statistical sample is taken from distributions of *Campylobacter* concentrations (in water and in food). Whether combining the doses that have been ingested during the day results in an overall increase or decrease of the probability of infection or not will depend on the actual doses, the dose-response model used and its parameters.

The probability of infection is determined with the dose-response curve (Figure 2). Note that infection does not necessarily cause illness; the relationship between these two is not well understood.

The key parameters of the model are listed in Table 1.

Recreational swimming

The probability of recreational swimming, the duration of the swim, the volume of water ingested during the swim, and the numbers of *Campylobacter* contaminating the water were all derived from data collected for the Ministry for the Environment Freshwater Microbiological Research Programme (FMRP, McBride et al. 2002). These data include 24 freshwater recreational sites distributed throughout New Zealand, from large rivers (e.g., the Waikato) to much smaller streams (e.g., the Pohangina). The MPN data on the numbers of *Campylobacter* present in the water was handled using a binning procedure described in the Appendix.

Drinking water

The volume of water consumed by an individual during a day was estimated as 2L per day, and it was assumed that this applied to all New Zealanders. It is acknowledged that much of this consumption will be as hot drinks, which will not contain *Campylobacter*: this has not been accounted for in the model, and so this figure represents a worst-case scenario.

The proportion of New Zealanders consuming the various grades of water (good, poor, ungraded) was based on data from ESR (Alan Ferguson, ESR Water Group, Christchurch Science Centre, pers. comm.) and data from water source grades. The probability that good or poor water is contaminated was considered low (0.0001 and 0.001), based on results from a survey of drinking waters, conducted by ESR for the Ministry of Health (Nokes et al. 2004). The probability that an ungraded water was contaminated by *Campylobacter* was rated at 0.04, based on data from testing roofwater supplies, provided by ESR as part of infectious intestinal disease investigations by HPOs.

Regarding the numbers of *Campylobacter* in each water type (if contaminated), it was decided to base this on data from environmental water sources tested as part of the FMRP (McBride et al. 2002). Adjustment factors of 1000 and 10 were applied to these results to account for the effect of water treatment prior to drinking (e.g., the concentration of *Campylobacter* in the "good" drinking water supply was taken as the FMRP result divided by 1000).

Food

Only poultry and red meat were included in the model as potential exposures. The probability that a person eats red meat or poultry on a given day, and the amounts eaten, were derived from National Nutrition Survey data reported in Risk Profiles (Lake et al. 2002; Lake et al. 2003).

The probabilities of contamination of red meat and poultry were derived from published data and a quantitative survey of retail products undertaken by ESR for the NZFSA (publication in preparation). The figure of 0.6 (Table 1) represents a composite probability intended to represent the variety of types of raw poultry on the market. The probability of contamination of red meat of 0.05 (Table 1) represents an overall probability of contamination of sheep, beef and pig meat.

The numbers of *Campylobacter* present per gram fresh weight (gfw) of red meat and poultry were decided in the light of results from the ESR survey. Results for poultry were reviewed and appeared sufficiently similar to the MPN *Campylobacter* per 100 mL of water results from the Freshwater Microbiology project that the latter could serve as a proxy (per gfw). There were fewer data for *Campylobacter* numbers on red meat as the prevalence is substantially less. While counts appeared lower, it is still possible that higher counts could appear as the number of positive samples increases. Consequently, it was decided to take a the same count distribution as was used for poultry. This will be reviewed as more data become available.

A two-step transfer from raw meat or poultry to ingestion during food handling was included, with transfer rates from a published study (Chen et al. 2001). The probability that a meat portion would be undercooked (0.04, Table 1) was based on the results of a telephone survey of New Zealander's cooking preferences (Thomson & Lake, 1995). The proportion of *Campylobacter* that might survive such undercooking was derived from the assumption that even a small amount of cooking would provide a 2 $\log_{10}$ reduction in bacterial numbers.

In developing the model we have assumed that there is no change in *Campylobacter* levels between the point of retail purchase and handling in the domestic kitchen (because the growth temperature range for this bacterium is 30–45 degrees Celsius). We assume that the majority of meat and poultry are at least refrigerated through the retail and domestic chain. Also, it appears that the majority of red meat is sold fresh (though some is subsequently frozen). Freezing will reduce *Campylobacter* numbers (by about 2 orders-of-magnitude) and this factor has been incorporated into the model.

Occupational exposure

This proved to be the most difficult exposure route to include. The proportion of the New Zealand population potentially exposed to livestock was derived from the proportion considered by Statistics New Zealand to be "rural". A further weighting (0.33) was included to account for the fact that not all rural New Zealanders will be exposed to livestock. A further factor (0.75) was included to cover the number of days where exposure did not occur. Detailed references for these figures are given in the footnotes to Table 1.

The number of bacteria in faecal material, and the amount of faecal material that might be ingested (through poor hygiene, cross contamination of food or cigarettes, etc.) was difficult to assess. As an interim approach the ingested amount was set to 0.0001–0.1 grams (using a uniform distribution). The range of concentrations of *Campylobacter* in animal faeces was taken from Stanley et al. (1998 & 2003).

2.2 *Campylobacter* Farm Environmental Model

The overall objective of this model is to examine the movement of *Campylobacter* through a farm in an area dominated by agricultural land use. The schematic model structure is shown in Figure 3. The purpose of the model is to simulate the main *Campylobacter* pathways on a hypothetical farm that is adjacent to a stream (see Table 2 for system details). The model tracks the flux of *Campylobacter* between the cows and the environment (dairy shed, pasture, and stream) (Figure 3) on an "average day" (e.g., it does not track variations in *Campylobacter* flux through time). The model was designed such that the impacts of various management strategies (e.g., fencing of the cattle from the stream, use of bridge to cross the stream, removal of the stream as a source of drinking water for the cattle, treatment wetlands, buffer strips) could be assessed in future simulations. For now, the basic performance of the model is presented. The potential influence the dairy operation has on *Campylobacter* in the environment is indicated by differences in *Campylobacter* concentrations in the stream above and below the farm. A key variable for this calculation is the density of *Campylobacter* in an infected cow's faeces, which has been estimated as between 70 MPN *Campylobacter* per gfw and 10^6 MPN *Campylobacter* per gfw (Stanley et al. 1998).[3] In addition, the amount of *Campylobacter* ingested by the herd will increase the proportion that is infected. We could not find information on the dose required to infect cows so we developed a series of relationships that would most likely bound the actual relationship between average number of *Campylobacter* ingested by the herd and proportion of the herd infected (Figure 4).

The hypothetical dairy farm characteristics (Table 2) used in the results reported here assume that routes of *Campylobacter* from the cattle to the environment include the dairy shed, paddock, and upstream sources (Table 2, Figure 3). Faecal matter deposited in the dairy shed is transferred to an ungrazed paddock through irrigation. This paddock is underlain by artificial drainage (tile drains) that connect to the stream. It is further assumed that there is no direct input of faecal material from the dairy shed to the stream (such as a drainage ditch). Cows are assumed to have access to the riparian area and must cross the stream when they are moved from the paddock to the dairy shed. They can defecate directly into the stream water.[4]

[3] "gfw" denotes grams fresh weight
[4] We note that this practice is being progressively reduced as enhanced on-farm management practices are being implemented.

3. Results and Discussion

3.1 *Campylobacter* Human Exposure Model

The results of this model are shown in Figure 5. This shows the estimated proportion of cases of infection caused by the individual exposures. Using the initial settings as described in Table 1, it was found that cross-contamination from poultry, and to a lesser extent, cross-contamination from red meat were the exposures that most frequently caused infection, followed in decreasing relative importance by occupational contact, drinking untreated water and recreational swimming. The remaining exposure routes—drinking good or poorly treated water and eating undercooked poultry or red meat—were relatively infrequent causes of infection (Figure 5). Eating undercooked red meat and drinking well-treated water had the lowest risk of infection than all other pathways. The relative importance of these sources (if not the pathways) is consistent with previous studies (e.g., Eberhardt-Phillips et al. 1997).

There are a number of factors that could be refined to more closely reflect real life. The greatest uncertainty is probably in assessing the occupational exposure. Refinement of this part of the model could include:

- creating separate populations and probabilities of contamination for different types of farm and animal;
- probability of unhygienic behaviour creating exposure (some interactions with contaminated animals will not cause exposure owing to hygienic practices of rural people);
- the effects of occupationally acquired immunity; and,
- seasonal factors.

We were unable to obtain data to incorporate these factors, but we have examined sensitivity to the manner in which occupational exposure has been modelled.

3.1.1 Model performance: Sensitivity to key parameters

The single parameter sensitivity method is commonly used to conduct sensitivity analysis on stochastic models (reviewed in Haefner 1996). It examines a model's sensitivity to input variables. In this method, the sensitivity index (S) is defined as the standardized change in a selected output parameter over the standardized change in a single input parameter while holding all other input parameters constant:

$$S = \left(\frac{R_a - R_n}{R_n}\right) \Big/ \left(\frac{P_a - P_n}{P_n}\right)$$

where R_a and R_n are the adjusted and nominal output parameters and P_a and P_n are the adjusted and nominal input parameters. When $S = 1$, the change in output equals the change in input. We used the mean number of cases infected per day as the output parameter, increased each of the selected input parameters by 10% of their nominal value,[5] and report the resulting value of S (Table 3).

The input parameters to which the model was most sensitive were the probabilities that poultry or red meat were contaminated.

The results of the sensitivity suggest that this model is rather insensitive to variations in most parameters. The most sensitive parameter was the shape parameter used in the bin selection method (Table 3), and which resulted in a 19.2% reduction of total number of individuals infected. However, since this parameter influences the contribution from *all* pathways equally, the relative importance of each pathway did not change from the base run (e.g., < 3% difference by pathway between the base and sensitivity run). The parameters dealing with food preparation and consumption, especially with poultry, were modestly sensitive parameters, followed by the parameters associated with occupational exposure (Table 3).

3.1.2 Model performance: Robustness against change in structure

The construction of any model requires that choices be made on the underlying structure. These choices in model framework can greatly influence the predicted results. The purpose of the robustness analysis is to assess the influence selected design choices in the model framework have on the model results. We have identified some design choices that we subjected to a robustness analysis. The robustness analysis consists of comparing model results from the current configuration with the results from an alternative design choice.

Summed Daily Dose versus Independent Dose Methods

In the model as reported (McBride et al. 2004), the total dose of *Campylobacter* for a given day for an average individual is the sum of doses obtained from all exposure

[5] This multiplier was also applied to the shape parameter for the geometric distribution in the *Campylobacter* bin selector (see the Appendix). The alternative (not done) would be to apply the multiplier to the dose received, which would be unlikely to cause much change in infection probabilities. In any event, all pathways would be affected similarly, as explained in Section 3.1.1.

pathways: recreational swimming, drinking water, eating undercooked meat, cross-over contamination from uncooked meat, and occupational hazard (exposure to livestock). The total daily dose is then used to determine the probability of infection using the dose-response curve, which is then used to determine if the individual is infected. This is the *Summed Daily Dose* method.

An alternative method in calculating the *Campylobacter* infection for a given individual would be to consider a separate probability of infection for each exposure pathway with a dose of at least one infectious *Campylobacter* and the individual would be "infected" if any of the pathways leads to an infection. Running the model in this mode (referred to hereafter as the *Independent Dose Method*) resulted in a 1.5% reduction in the number of infected individuals per day as compared to the *Summed Daily Dose* method. This suggests that the decision to use the Summed *Daily Dose* method instead of the *Independent Dose Method* had very little influence on model results.

Using the *Summed Daily Dose* method, the vast majority (93.12%) of all infections were from the dose from one exposure pathway (Table 4), with 78.55% of single-pathway infections from the two cross-contamination exposure pathways (Table 5). The model framework separates the exposure pathways of cross-contamination from meat storage and preparation (for poultry and red meat) prior to cooking and the exposure pathways from eating undercooked meat. So, even with the summed dose method used in the model, obtaining a dose of *Campylobacter* from eating undercooked meat and from meat cross-contamination was rare. In fact, exposure from 2 or more pathways occurred in only 7.85% of all cases (Table 4). However, of the proportion of two-exposure pathway infections, all of the cases were associated with either cross-contamination from poultry or cross-contamination from red meat (Table 6).

Other Robustness Measures

1. Applying the water bin boundaries to pathways other than recreational swimming. We think this would be a good choice since it is central to the model and the group had a discussion on the validity of this approach. However, we stuck with this method because there simply isn't enough data to create equivalent distributions for the other exposure pathways.[6]

[6] Maybe the easiest way to test this one is to question the assumption that the number of *Campylobacter* per gfw is equivalent to the number per 100 mL.

2. For the meat pathways, we determined the dose based on grams of meat consumed and determined dose using numbers of *Campylobacter* per gram. What if we compare this to surface area of meat and determined the dose as number per cm^2? This is not expected to add much value, but could be investigated.

3. Observations that may fall best in a validation/verification section—does the model underestimate known rates of infection by exposure pathway such as recreational swimming and drinking water? Note however that this is hard to check. For example, the Freshwater Microbiological Research Programme offered a set of calculations implying that about 4% of cases of *Campylobacter* infection or illness could be attributable to contact with recreational freshwater, whereas our model predicts this percentage to be about 1%. Such differences could merely reflect the different set of assumptions made in each study.

3.2 *Campylobacter* Farm Environmental Model

The relative importance of occupational contact and freshwater swimming as *direct* exposures is relatively small as compared to exposure to contaminated meat products (Figure 5, Eberhardt-Phillips et al. 1997, McBride et al. 2002). However, New Zealand's reported high rate of campylobacteriosis may be influenced *indirectly* by the persistence of *Campylobacter* over a large proportion of the New Zealand landscape. New Zealand has twelve times the world's areal average of combined sheep and goats and three times the world's average for cattle (Taylor & Smith 1997), and sheep and cattle at least can carry *Campylobacter*. In addition, 51% of New Zealand is pasture, which is twice the world's average (Taylor & Smith 1997) and therefore, approximately half of New Zealand is potentially subjected to faecal deposition of domestic animals that can potentially carry *Campylobacter*. Furthermore, this land is the more easily accessible.

Campylobacter has been detected in numerous freshwater environments throughout New Zealand environment (Savill et al. 2001, McBride et al. 2002, Eyles et al. 2003). These studies suggest that *Campylobacter* is common in the aquatic environment, typically in low concentrations, but with occasional high values particularly when water is more turbid than at baseflow.

Results from the **Water_Simple Model** suggest that dairy (and other) farms are potentially an important source of *Campylobacter* in the stream environment (Skelly 2002), which has provided the motivation to develop the ***Campylobacter* Farm Environmental Model**. The results from the latter model suggest that infected cows defecating in the stream can have a substantial impact on *Campylobacter* concentrations in the stream (Figure 6). The relative importance of paddock runoff has yet to be fully investigated. In addition, a high proportion of the herd can potentially become infected from drinking stream water of low to moderate *Campylobacter* concentrations (Table 7). Together, these results suggest that cows are potentially a major source of environmental contamination of *Campylobacter* and they may even be capable of contaminating the land environment to levels great enough for their own re-infection. Sensitivity studies (Table 7) have shown that the dose required for cattle to become infected (from the dairy shed, from grazing and from drinking stream water) is a key variable.

3.3 Information Gaps

During the development of the models described within this report, several areas of data or knowledge deficiency have been identified. The identification of such areas using a structured modelling methodology is a valuable tool for the effective and efficient targeting of future research. Furthermore, this research may be prioritised by identifying which of these data deficient variables has the most influence on the model output.

The following knowledge gaps were found while making the models:

- Factors involved in occupational exposure (the ***Campylobacter* Human Exposure Model** is somewhat sensitive to variables associated with this factor; more importantly, we have less secure means of modelling this exposure pathway).
- Human dose-response, especially the chance of infection at low doses, and the dose-response for multiple strains of *Campylobacter* and for *Campylobacter* species other than *C. jejuni*.
- Animal dose-response (the ***Campylobacter* Farm Environmental Model** needs better data on this aspect).
- Immunity from repeat exposures, especially by farm workers.
- Better data on the numbers of *Campylobacter* on red meat.
- Prevalence and concentration of *Campylobacter* in farm animals.

3.4 Next Steps?

The occupational exposure route could be refined to improve the ***Campylobacter* Human Exposure Model**. It would also be desirable to incorporate additional exposure routes such as other types of food (including raw milk), pets, and overseas travel. Basic concepts such as amounts ingested and direct/indirect routes from animals to humans need further consideration.

Factors related to meat and poultry handling could be added. The issue of relative numbers of *Campylobacter* on meat compared to poultry needs to be resolved. Including historical information on changes in proportions of meats sold fresh or frozen and total meat consumption could enable us to predict a temporal trend in *Campylobacter* infection.

Although the ***Campylobacter* Farm Environmental Model** has proved to be useful in conceptualising the feedback between livestock and the environment, it is currently in an early stage of development and could be expanded to include more realistic management scenarios, and be expanded to include all forms of farming in New Zealand. We would like to carry its development further by placing it in an Monte Carlo framework, which would allow us to incorporate the uncertainties into the hypothetical framework.

3.5 Main Findings Thus Far

We have *tentatively* concluded that cross-contamination during preparation or storage of poultry, and to a lesser extent red meat, are the most important exposures. As noted above, the importance of cross contamination from red meat will depend on whether the assumption that the number of bacteria present is the same as on poultry is correct. The least important exposure route was drinking well-treated water. Occupational contact with livestock was also identified as important, and this exposure route was identified as important for rural populations in a cohort study conducted in Ashburton (Baker et al. 2002). Relative risks of infection from the remaining exposures were low, compared to cross-contamination from poultry.

Given the potential importance of the tentative findings in this work, the two models developed thus far in this project should be more fully assessed and expanded to better account for uncertainty in some inputs (many of which are currently at fixed values). Also, the environment model should be expanded to include more complex landscapes, more sources (other animal species) and more routes for *Campylobacter*,

with a view to more fully assessing both the efficacy of possible mitigation measures, and the sources and routes of contamination of water and foods.

A reduction of on-farm contamination is likely to result in less contamination of water, and possibly food, thus reducing exposures. This should now be happening in dairying areas, with progressive implementation of Fonterra's *Dairying and Clean Streams Accord*. The relationship between environmental contamination and animal infection is likely to be complex, and involve multiple exposure routes. This makes the control of *Campylobacter* contamination difficult, particularly on chicken broiler farms.

An alternative is to reduce contamination of food during processing, and it should be noted that a New Zealand poultry food chain quantitative model is being developed by ESR for the NZFSA. The model will not only quantify the fate of *Campylobacter* through the poultry food chain but will enable assessment of the effect of various processing interventions on *Campylobacter* exposure. Several intervention-based research projects are currently being funded by the NZFSA and poultry industry.

4. Acknowledgements

We are grateful for the financial support from the Ministry of Health and PIANZ for this project, and for the various studies initiated by NZFSA and PIANZ. A number of colleagues provided useful information.

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Table 1. Variables used in the *Campylobacter* Human Exposure Model.

Variable Description	Value	Source
Recreational Swimming		
Duration of swim (hr /day)	0.5 (0.25 – 2.0)	1
Volume ingested (mL/hr)	50 (10 – 100)	1
Proportion of New Zealanders that swims	0.0625	1
Number of swim events per swimmer (in a year)	1–20	1
Drinking water		
Volume consumed (L)	2	2
Proportion of New Zealanders that drink good water	0.75	2
Proportion of New Zealanders that drink poor water	0.22	2
Proportion of New Zealanders that drink ungraded or untreated water	0.03	3
Probability good water is contaminated	0.0001	2
Probability poor water is contaminated	0.001	2
Probability ungraded or untreated water is contaminated	0.04	4
Adjustment factor used to calculate dose for good water	1000	2
Adjustment factor used to calculate dose for poor water	10	2
Food		
Proportion of New Zealanders that eats poultry of a given day	0.21	5, 6
Proportion of New Zealanders that eats red meat on a given day	0.78	5, 6
Proportion of New Zealanders that eat neither red meat or poultry on a given day	0.01	5, 6
Probability that poultry is contaminated	0.6	7
Probability that red meat is contaminated	0.05	7
Proportion of *Campylobacter* on poultry that survives cooking	0.01	2
Amount of poultry consumed on a "poultry day" (kg/day)	0.125	5, 6
Amount of red meat consumed on a "red meat day" (kg/day)	0.1000	5, 6
Proportion of *Campylobacter* transferred from poultry to cooking surfaces	0.1000	8
Proportion of *Campylobacter* transferred from cooking surfaces to other foods	0.1000	8
Proportion of *Campylobacter* transferred from red meat to cooking surfaces	0.1000	8
Proportion of New Zealanders that prefer undercooked meat	0.04	9
Proportion of *Campylobacter* on red meat that survives cooking	0.0100	2
Proportion of poultry frozen before preparation	0.34	10
Campylobacter reduction factor for frozen poultry	100	7
Occupational Exposure		
Probability person is a rural New Zealander	0.1429	11
Proportion of rural population exposed to livestock	0.3333	11
Proportion of the year exposed to livestock	0.7500	2
Probability farm is contaminated with *Campylobacter*	0.8000	2
Amount of faecal material ingested per event (gram)	0.0001–0.1	2

[1]McBride et al. 2002; [2]Authors' consensus based on first principles; [3]Alan Ferguson, ESR Water Group, Christchurch Science Centre, pers. comm. 2004; [4]Andrew Ball, ESR Water Group, Christchurch Science Centre, pers. comm.; [5]Lake et al. 2003; [6]Lake et al. 2002; [7]Rob Lake, ESR, Christchurch Science Centre; [8]Based on Chen et al. 2001; [9]Thomson and Lake 1995; [10]Cooper-Blanks (1999); [11]New Zealand Statistics 2001.

Table 2. Variables used in the *Campylobacter* Farm Environment Model.

Variable	Value	Reference
Livestock characteristics		
number of cattle	200	1
Faecal output per cow (kg / day)	11.28	2
Campylobacter concentration (cnt / gfw faeces), for infected stock	70 (up to 10^6)	3, 10
Mean volume water ingested (L per drinking event)	10	4
Proportion of cows that drink during a stream crossing	0.2	4
Number of stream crossings per day	4	2
Stream characteristics		
Mean velocity (m / s)	0.5	5
Reach length (m)	100	5
Mean wetted width (m)	10	5
Mean wetted depth (m)	0.25	5
Mean cross-section area (m^2)	2.5	5
Mean discharge (m^3/ s)	1.25	5
Stream daily volume (m^3)	108000	5
Campylobacter concentration upstream of farm (cnt / 100mL)	24	6
Fate of the daily faecal production by the herd (%):		
Deposited in the dairy shed	10	7
Deposited in the stream	8	2,8
Deposited on the paddock	82	9
Fate of the daily faecal production in the dairy shed (%)		
Ingested by cows	0.00001	9
Irrigation to the paddock	90.0000	9
Directly into the stream	0.0000	5
Other losses	9.9999	9
Fate of the daily faecal load on the paddock (%)		
Ingested by cows	0.00001	9
Runoff (tile drain) to stream	10.0000	9
Other losses	89.9999	9

[1]Dr. Rob Collins, NIWA Hamilton, personal communication; [2]Dr. Rob Davies-Colley, NIWA Hamilton, personal communication; [3]Stanley et al. 1998; [4]John Nagels, NIWA Hamilton, personal communication; [5]Reasonable values for a mid-sized stream; [6]Eyles 2003; [7]Sukias et al. 2001; [8]Collins and Rutherford 2004; [9]Authors consensus based on first principles; [10]Stanley and Jones 2003

Table 3. Sensitivity values (S) for each singe-parameter sensitivity test conducted on input parameters, absolute value of parameters ranked from largest to smallest.

Variable Description	S	Rank
Bin selection method, geometric distribution shape parameter	–1.61	1
Probability that poultry is contaminated	0.52	2
Proportion of poultry frozen before preparation	–0.28	3
Probability that red meat is contaminated	0.25	4
Proportion of *Campylobacter* transferred from cooking surfaces to other foods	0.19	5
Amount of poultry consumed on a "poultry day" (kg/day)	0.17	6
Proportion of *Campylobacter* transferred from poultry to cooking surfaces	0.17	6
Proportion of rural population exposed to livestock	0.15	7
Probability person is a rural New Zealander	0.13	8
Occupational exposure – amount faecal material ingested	0.11	9
Proportion of the year exposed to livestock	0.10	10
Probability farm is contaminated with *Campylobacter*	0.07	11
Amount of red meat consumed on a "red meat day" (kg/day)	0.07	11
Proportion of *Campylobacter* transferred from red meat to cooking surfaces	0.07	11
Probability ungraded or untreated water is contaminated	0.03	12
Campylobacter reduction factor for frozen poultry	-0.03	13
Proportion of New Zealanders that prefer undercooked meat	0.02	14
Number of swim events per swimmer (in a year)	0.01	15
Volume consumed (L)	0.01	15
Duration of swim (hr /day)	0.00	16
Volume ingested (mL/hr)	0.00	16
Proportion of New Zealanders that swims	0.00	16
Probability good water is contaminated	0.00	16
Probability poor water is contaminated	0.00	16
Adjustment factor used to calculate dose for good water	0.00	16
Adjustment factor used to calculate dose for poor water	0.00	16
Proportion of *Campylobacter* on poultry that survives cooking	0.00	16
Proportion of *Campylobacter* on red meat that survives cooking	0.00	16

Table 4. The mean daily infection associated with the number of exposure pathways predicted from two infection calculation methods used to determine an individual infection.

Number of Pathways	Proportion of all Infections (%)	
	Summed Daily Dose Method	*Independent Dose Method*
1	93.12	92.06
2	6.88	7.85
3	0.00	0.10
4	0.00	0.00

Table 5. The relative importance of an exposure pathway for infections that include a given pathway simulated for each of the infection calculation methods.

Exposure Pathways	Exactly 1 Pathway (%)	
	Summed Daily Dose Method	*Independent Dose Method*
Poultry cross-contamination	57.28	57.55
Red meat cross-contamination	21.27	23.34
Occupational contact	15.89	13.98
Poultry	3.09	1.91
Untreated drinking water	1.24	1.51
Recreational swimming	0.44	0.80
Red meat	0.79	0.70
Poor drinking water	0.00	0.20
Good drinking water	0.00	0.00

Table 6. The proportion of mean daily infections predicted by model for infections from exactly two exposure pathways for the *Summed Daily Dose* method (6.08% of all infections, Table 2).

Exposure Pathways	Exactly 2 Pathways (%)
Poultry, poultry cross-contamination	47.95
Occupational contact, poultry cross-contamination	26.03
Red meat and red meat cross-contamination	12.33
Occupational contact and red meat cross-contamination	9.59
Recreational swimming and poultry cross-contamination	2.74
Untreated drinking water and poultry cross-contamination	1.37

Table 7. Proportion of the herd infected with *Campylobacter* from drinking from the stream as a function of *Campylobacter* concentration in the stream (excludes ingestion from the paddock and dairy shed). The series are those defined in Figure 4.

Upstream concentration [organisms (100 mL)$^{-1}$]	Dose-response series			
	A	B	C	D
3	33	13	10	0
24	58	30	73	8
150	78	52	98	57

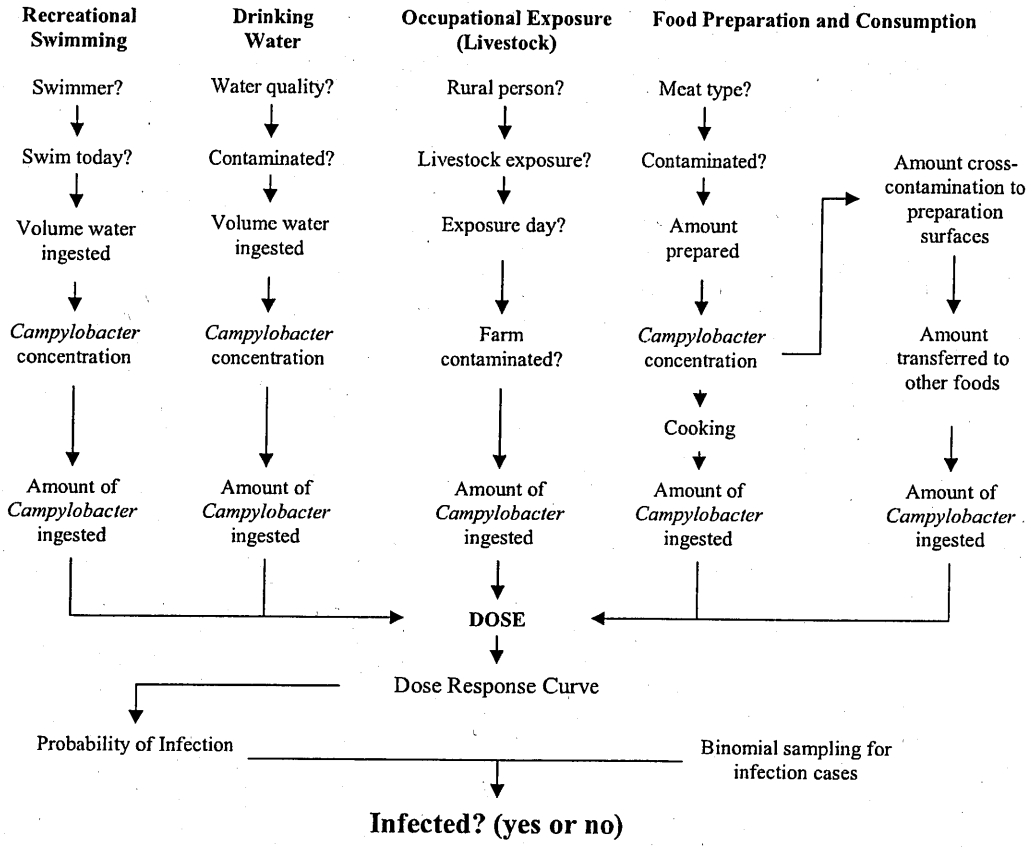

Figure 1. Structure of the *Campylobacter* Human QRA Exposure Model.

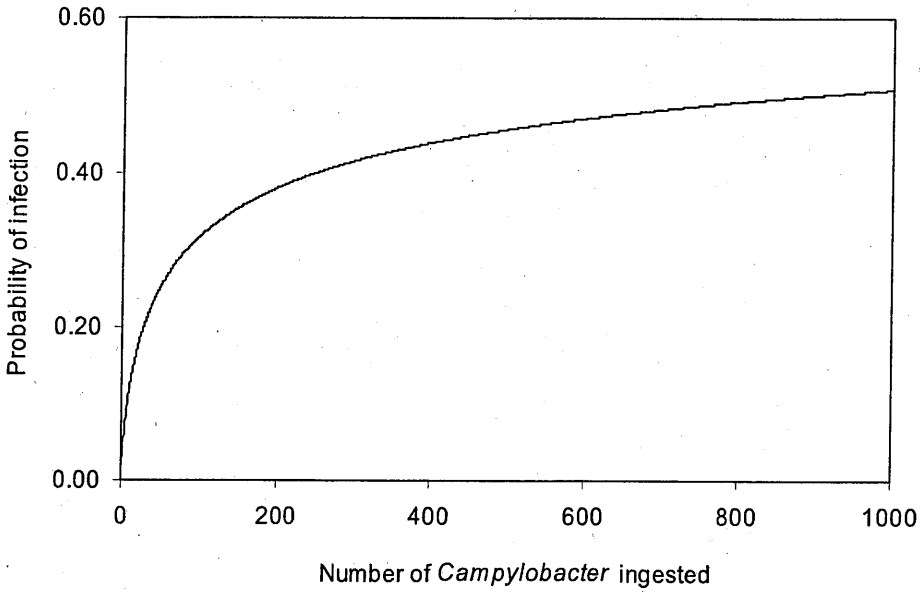

Figure 2. Dose-response curve used in the *Campylobacter* QRA Human Exposure Model. This is a "beta-Poisson" curve: Prob(Infection) = $1 - (1 + d/\beta)^{-\alpha}$, where $\alpha = 0.145$ and $\beta = 7.589$—in which case the median infective dose is $\beta(2^{1/\alpha}-1) = 897$—and d is the dose ("Number of *Campylobacter* ingested). This curve is taken from Medema et al. (1996), who fitted a beta-Poisson curve to clinical trial data reported by Black et al. (1988).

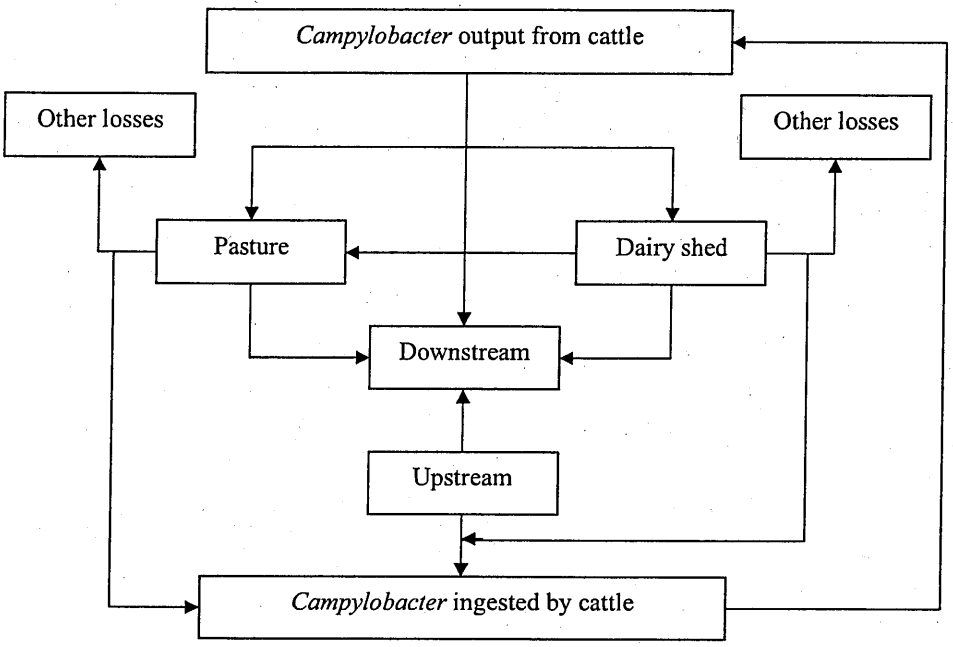

Figure 3. Pathways used in the *Campylobacter* Dairy Farm Model.

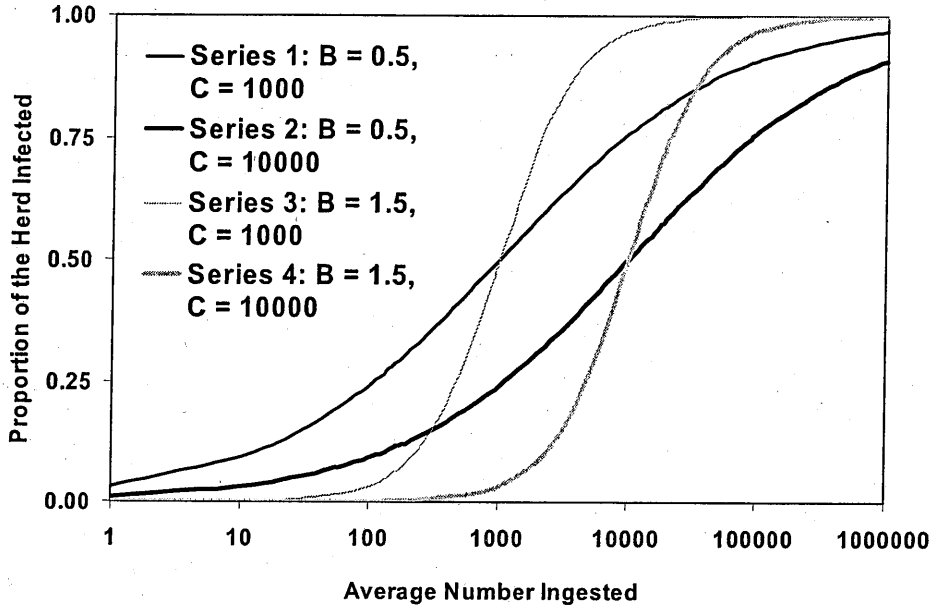

Figure 4. Infection curves used in the *Campylobacter* Farm Environmental Model, which relate the proportion of the herd infected as a function of the average number of *Campylobacter* ingested in a given day. The series are defined by the Hill equation $Y = A\ (N^B)/(C^B + N^B)$, where N = average number of *Campylobacter* ingested, A sets the upper limit ($A = 1$ for all series), B is a shape parameter, and C is the value of N where 50% of the herd is infected. The four series have been used in a sensitivity analysis.

This page replaces p. 27 of the report:

McBride, G.B.; Meleason, M.; Skelly, C.; Lake, R.; van der Logt, P.; Collins, R. (2005). Preliminary relative risk assessment for *Campylobacter* exposure in New Zealand: 1. National model for four potential human exposure routes; 2. Farm Environmental Model. NIWA Client Report HAM2005-094, project MOH05203. Report to Ministry of Health and Enteric Disease Research Group Steering Committee, 31 p.

The figure itself is unchanged, but the legend and caption have been amended.

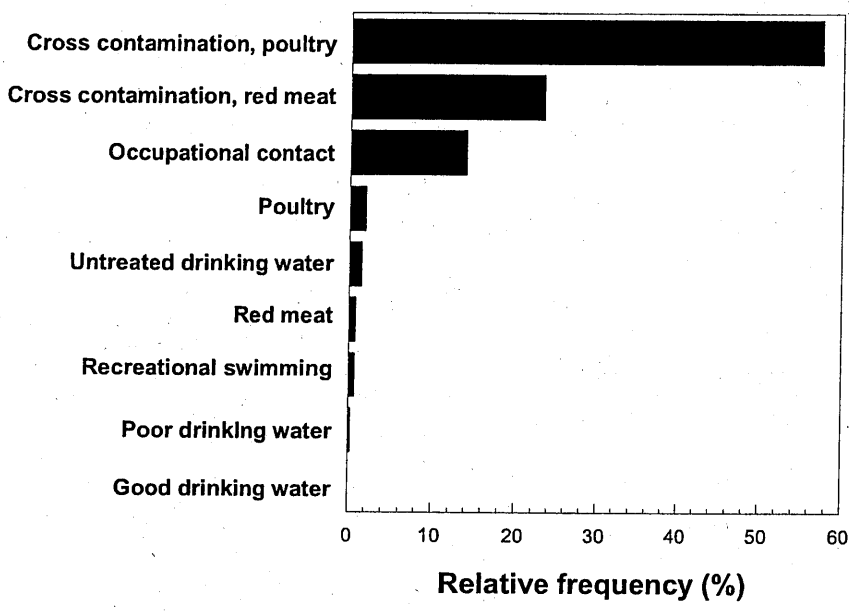

Figure 5. Relative frequency of the various pathways to infection from the *Campylobacter* Human Exposure Model.

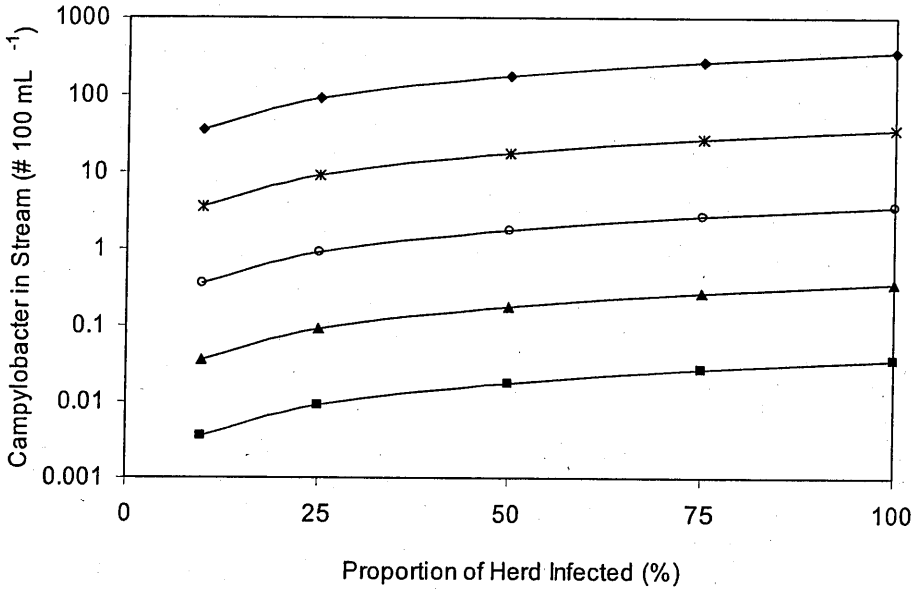

Figure 6. The concentration of *Campylobacter* in the hypothetical stream from direct deposition from the cows (8% of total daily faecal load) as a function of the predicted proportion of the herd infected (see Table 3 for details on the stream and herd characteristics). *Campylobacter* concentrations were calculated based on total flow over a 24-hr period. The symbols represent different levels of *Campylobacter* concentrations in the faecal material (organisms gfw^{-1}): (■) 10^2; (▲) 10^3; (○) 10^4; (✳) 10^5; (◆) 10^6.

6. Appendix

6.1 Sampling the *Campylobacter* MPN distribution

The histogram in the top part of Figure A.1 displays *Campylobacter* results for 726 water samples, expressed as MPN per 100 mL, from the Freshwater Microbiology Research Programme (FMRP) (McBride et al. 2002). Sampling such a distribution is problematical, because:

- Each MPN value has a different "occurrence probability",[7]
- The data's distribution is multi-modal.

These problems are neatly overcome by a "binning" procedure. We define bins, using the criterion that each should contain two, and only two, MPNs with occurrence probabilities greater than 0.2. For the *Campylobacter* data the resulting boundaries of the bins are at 0, 0.15, 1, 4, 25, 110 and 2000 per 100 mL (the last figure has been elicited from microbiologists). The frequencies in each bin are then collected, as shown by the vertical open rectangles in the second part of the Figure, to which a distribution is fitted—a geometric distribution. The thin bars show this distribution's probability mass function, which is used on each Monte Carlo trial to select a bin number.[8] Having selected that bin, a random sample is taken between its floor and roof, using the uniform distribution.

For the FMRP data this works extremely well. For *Campylobacter* data in chicken we have similar data, expressed as MPN per gram. We have made the assumption that this distribution of *Campylobacter* in chicken is the same as that in the water samples in the FMRP, merely by replacing "per 100 mL" with "per gram". This is the best that can be done until such time as more detailed data are made available.

[7] That is, some MPN values are more likely than others when sampling a large number of samples with random distributions of microorganisms; none are equally likely.
[8] If a bin number greater than 5 is selected it is set to be bin 5 (these bins all contain the "greater than" data).

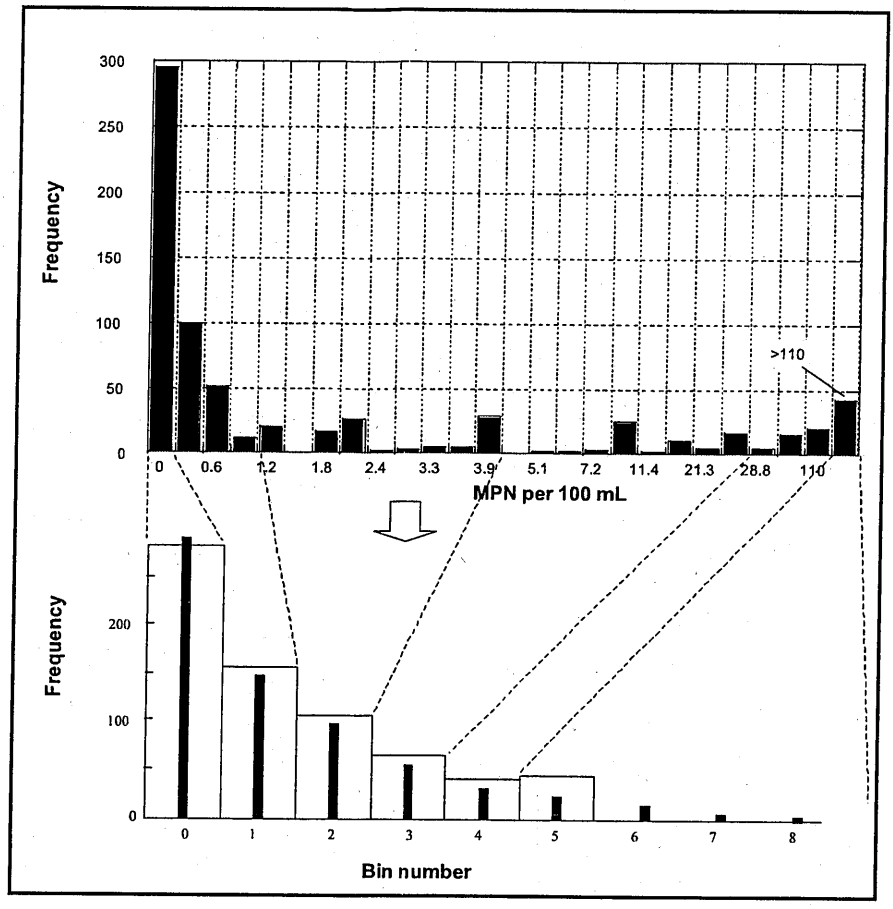

Figure A.1. Bin definitions for the frequency of *Campylobacter* per 100 mL of stream water.