

CARMA: A MULTIDISCIPLINARY PROJECT TO REDUCE RISKS OF CAMPYLOBACTERIOSIS

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Introduction

Campylobacter infections pose a serious public health problem in the Netherlands. On a population of approximately 16 million, they result in approximately 80,000 cases of gastro-enteritis per year, of which 18,000 cases see a general practitioner and with a most likely value of 30 fatal cases per year, mainly among elderly. In addition, there are about 60 cases of Guillain-Barré syndrome and 1400 cases of reactive arthritis and 10 cases of inflammatory bowel disease. Collectively, these disease endpoints result in an annual loss of 1200 healthy life years. The economic losses in the year 2000 are estimated at € 20 million per year (Mangen *et al.*, 2004).

The most important reservoirs of Campylobacter are found among animals, including farm animals, wild animals and pets. These reservoirs continuously contaminate the human environment, including the domestic environment and food products, hereby creating many pathways by which humans can come in contact with Campylobacter. Different research methods have been used, both nationally and internationally, to evaluate the relative importance of different exposure pathways, including case-control studies, microbiological analyses of patients and putative reservoirs, the typing of isolates of different origins, and statistical methods (Havelaar, 2002). Many studies have indicated chicken to be an important source of contamination, but this is by no means the only important contamination route. Other identified risk factors are meat from pigs and cattle, raw milk, direct contact with animals, water, and foreign travel.

Effective prevention of human campylobacteriosis requires a well-balanced set of measures. To this aim, the CARMA (Campylobacter Risk Management and Assessment) project has been started in 2001. The goal of the project is to advise on the effectiveness and efficiency of measures aimed at reducing campylobacteriosis in the Dutch population. This goal is reached by providing scientific support to a risk management process, as defined by the Codex Alimentarius Commission on Food Hygiene (Anonymous, 2001). Risk managers are the Ministry of Health, Welfare and Sports and the Ministry of Agriculture, Nature and Food Quality. This paper describes the framework of the CARMA project, and presents some preliminary results.

The goal of CARMA is to advise on the effectiveness and efficiency of measures aimed at reducing campylobacteriosis in the Dutch population. The key questions to be evaluated are:

- What are the most important routes by which the Dutch population is exposed to Campylobacter and can the contribution of these routes be quantified?
- Which (sets of) measures can be taken to reduce the exposure to Campylobacter, what is their expected efficiency and societal support?

Design of the CARMA project

In the first (completed) phase, all available information on campylobacteriosis was collected and summarized in an extensive risk profile (Havelaar, 2002). This information is used in later phases to assess the relative contribution of different sources of contamination to the incidence of human *Campylobacter* infections (see following paragraphs). A risk model will be build for each major route of infection, Currently, the focus is on the broiler meat chain only, because of limited time and resources. Figure 1 shows the general approach that will be used to evaluate the effectiveness and efficacy of possible interventions.

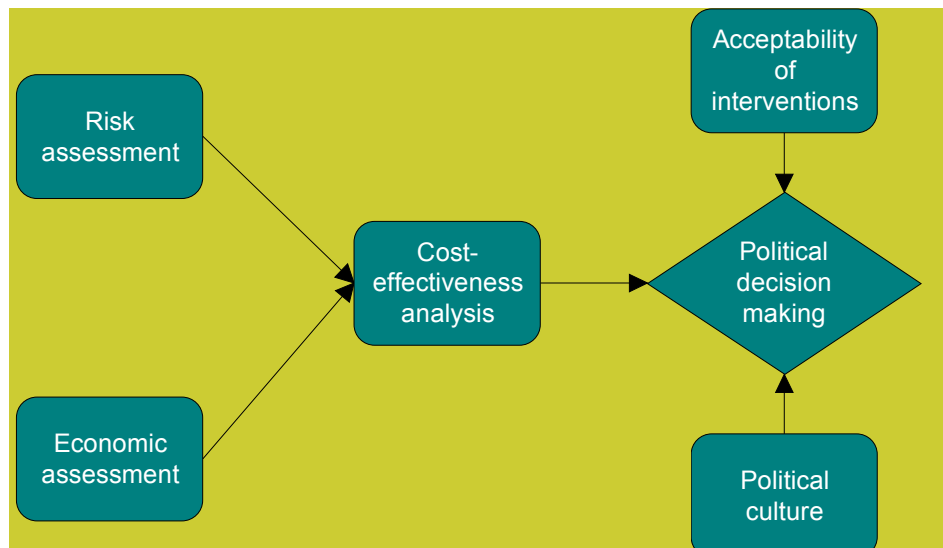


Figure 1. Design of the CARMA project.

A risk model describes the transmission of *Campylobacter* for the particular contamination route and combines the resulting exposure estimate with dose-response information in order to assess the incidence of *Campylobacter* infections. In a disease burden model (part of the economic assessment), different outcomes related to these infections, including gastro-enteritis, Guillain-Barré syndrome, reactive arthritis, inflammatory bowel disease and mortality, are quantified. The combined disease burden of these end-points is expressed in Disability Adjusted Life Years (DALYs). The economic assessment further evaluates the cost of illness due to *Campylobacter* infections in the starting situation. In consultation with risk managers and stakeholders, a series of intervention measures has been selected (see Table 1). The effects of these measures on the incidence of infection (risk model), disease burden of related illnesses (disease burden model) and associated cost of illness (economic model) are estimated. In addition, the costs associated with the implementation of intervention measures are evaluated in the economic model. All information collected, including reduced disease burden and its associated savings, as well as costs of interventions to be implemented, are combined in the cost-effectiveness analysis. Here, different interventions are compared based on several criteria including the absolute reduction in number of cases of illness or death, the absolute increase or decrease in production costs, the (net) costs per case of illness or death averted and the costs per (quality adjusted) life year gained. This allows *a priori* evaluation of

different sets of intervention measures. As many necessary data are lacking, uncertainty analysis will be an important aspect of the work, and for some interventions only sensitivity analyses will be possible. Absolute effects, costs and cost-effectiveness ratios are important elements of information to support risk management decisions. However, societal and political factors also have a major effect on decision-making. Therefore, in the project these factors are also described and presented to decision-makers. For more details, see Bogaardt et al. (2004).

Table 1. Interventions in the broiler meat chain

Interventions at the farm

1. Discontinuation of thinning
2. No other farm animals in combination with broilers
3. Improved hygiene
4. Phage therapy

Interventions during processing

5. Logistic slaughter
6. Reduce fecal leakage during processing
7. Decontamination of the scald tank
8. Chemical decontamination of carcasses
9. Surface decontamination of carcasses by heat
10. Surface decontamination of carcasses by crust freezing
11. Decontamination by e-beam irradiation
12. Freezing of chicken meat
13. Channeling and 6
14. Channeling and 7
15. Channeling and 8
16. Channeling and 9
17. Channeling and 10
18. Channeling and 11
19. Channeling and 12
20. Channeling and heat treatment of meat from positively tested flocks

Interventions in the consumer phase

21. Consumer education
 22. Freezing of chicken meat by consumers
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Currently, evaluation of interventions is in full course. Results on logistic slaughter have been reported (Havelaar et al., 2004^{a,b}).

Comparing the exposure to Campylobacter by various routes

To attribute human campylobacteriosis to different sources, epidemiological methods have mainly been used. Worldwide, a number of case-control studies have been carried out, and many sources have been identified. However, the sources and attributable fractions identified in these studies may differ or may even be conflicting. Some studies, for example, have identified the consumption of chicken meat as a risk factor, whereas other studies have identified this as a protective factor.

An alternative method for source attribution is based on risk assessment techniques. In the CARMA project, all available information on occurrence of Campylobacter in putative sources was combined with data or estimates on intensity of contact with

sources to produce comparative exposure estimates (Evers et al., 2004). Thirty-one routes were considered. These were:

- Consumption of food (prepared or raw)
 - Chicken, turkey, pig, beef, milk, sheep, fish, shellfish, vegetables and fruit (19 routes)
- Direct contact with animals
 - Pets, farm animals, petting zoo (9 routes)
- Water
 - Recreational water, drinking water (3 routes)

The method used for calculating exposure was straightforward. For foods, for example, exposure was the product of:

$$\begin{aligned} & \text{the amount of food ingested per person per day (average over the total population)} \\ & \quad \times \\ & \quad \text{the prevalence of contaminated products at the retail level} \\ & \quad \quad \times \\ & \quad \quad \text{the concentration of Campylobacter in contaminated products} \\ & \quad \quad \quad \times \\ & \quad \quad \quad \text{the fraction surviving after heating (including the fraction reaching the consumer by} \\ & \quad \quad \quad \text{cross-contamination).} \end{aligned}$$

Exposure abroad was not considered. Many parameters were highly uncertain, and this was accounted for by using probability distributions and Monte Carlo simulation. Results are shown in Figures 2 and 3.

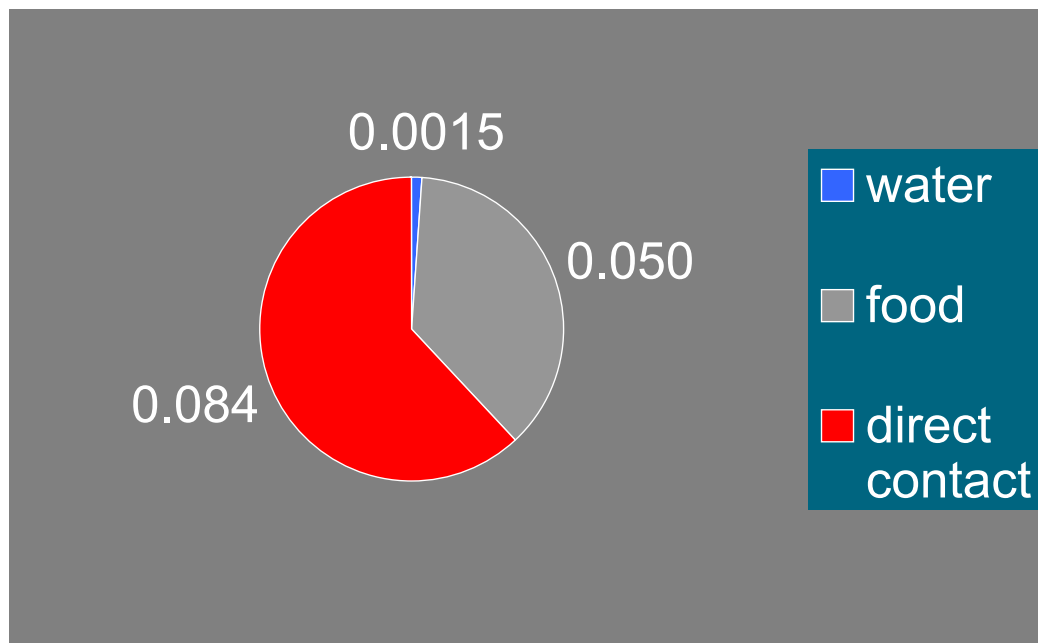


Figure 2. Average exposure of the Dutch population to Campylobacter for major groups of sources (Campylobacter cfu per person per day).

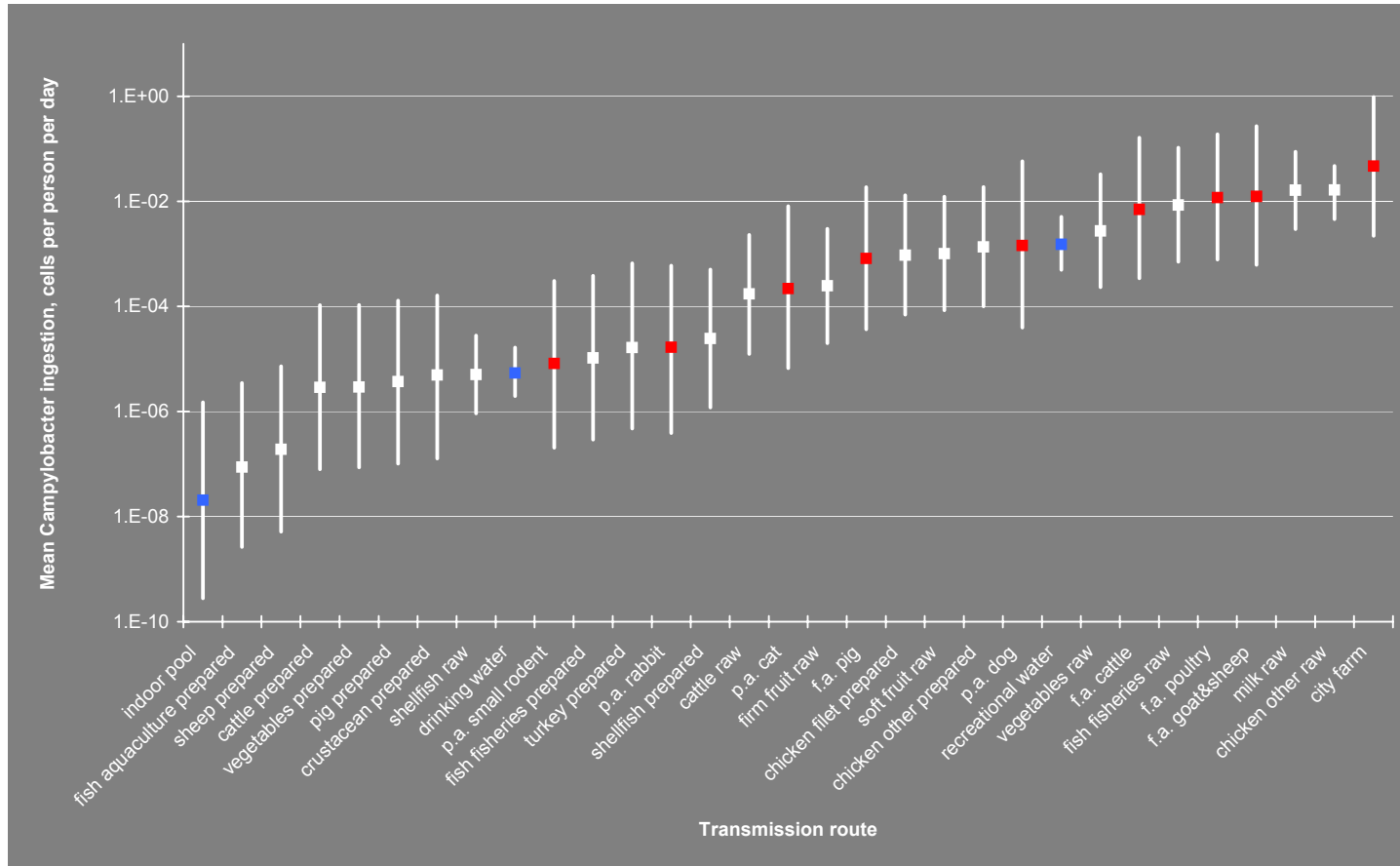


Figure 3. Average exposure of the Dutch population to *Campylobacter* (cfu per person per day, 2.5, 50 and 97.5 percentiles) for 31 different routes.

Average exposure totals 0.135 cfu per person per day, of which approximately 2/3 by direct contact with animals and 1/3 by food. Among food sources, raw foods such as non-pasteurized milk, fish (mainly herring in the Dutch case) and vegetables appear to be relatively important despite the relatively low prevalence of contamination. This is mainly due to the fact that the absence of a heating step that inactivates vegetative bacteria.

The relative exposure cannot be translated on a 1:1 basis into illness. Exposure to many important sources is highly clustered. For example, contact with farm animals is typical for farmers, abattoir personnel etc., but not for the general population. Also, some people will tend to drink raw milk regularly, whereas other may never do so. Moreover, clustering of exposure may lead to some degree of immunity that may significantly influence the outcome of exposure. As an illustration, we have calculated that a straightforward risk characterization using the dose-response model described by Teunis and Havelaar (2002), would predict 10 million cases of infection and 3 million cases of illness per year. Epidemiological studies observe only 80.000 cases per year. It is unlikely that the dose-response model overestimates the risk of infection and illness, as it was based on experiments using healthy adult volunteers who were exposed to a laboratory-adapted strain (Black et al., 1988).

Due to the considerable uncertainties and the confounding effects of immunity, exposure modeling does not yet appear to be a useful tool for source attribution of campylobacteriosis. It is likely that the effects of clustering and immunity also confound the results of case-control studies. Further understanding of the impacts of these phenomena on risks of illness and infection is of critical importance for reliable attribution of foodborne risks to various sources. The results do underline, however, that campylobacteriosis is a multi-source problem, and that preventive measures must be directed to all relevant sources.

Acknowledgements

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