参考資料9

CAMPYLOBACTER RISK MANAGEMENT AND ASSESSMENT

CARMA

RIVM report 250911006/2005

Risk assessment of Campylobacter in the Netherlands via broiler meat and other routes

M.J. Nauta[1], W.F. Jacobs-Reitsma[2], E.G. Evers[1], W. van Pelt[1], A.H. Havelaar[1*]

[1]National Institute for Public Health and the Environment (RIVM), P.O. Box 1, 3720 BA Bilthoven
[2] Wageningen UR, Animal Sciences Group (ASG), P.O. Box 65, 8200 AB Lelystad

[*] corresponding author
Microbiological Laboratory for Health Protection
e-mail: Arie.Havelaar@rivm.nl

This investigation has been performed by order and for the account of the Ministry of Public Health, Welfare and Sports, the Ministry of Agriculture, Nature and Food Quality, and the Food and Consumer Product Safety Authority, within the framework of project V/250911, CARMA: Campylobacter Risk Management and Assessment.

Het rapport in het kort

Risicoschatting van Campylobacter in Nederland via kippenvlees en andere routes

Elk jaar worden mensen ziek door de *Campylobacter* bacterie. Omdat de overheid wil weten wat zij hier het best tegen kan doen, is dit in het CARMA project onderzocht. Dit rapport beschrijft om te beginnen wat de oorzaken van campylobacterbesmetting zouden kunnen zijn. Direct contact met (huis-)dieren en de consumptie van onverhit voedsel komen naast kippenvlees als belangrijke bronnen naar voren. Kippenvlees zou een aanzienlijk deel van de ziektegevallen kunnen veroorzaken. Er is een wiskundig model gebouwd om meer inzicht te krijgen in het vóórkomen en de verspreiding van campylobacter in de productieketen van kippenvlees, van de boerderij tot en met de bereiding van het vlees in de keuken thuis. Met het model is ingeschat waar en hoe het best ingegrepen kan worden om campylobacter te bestrijden met als doel het aantal zieken dat erdoor veroorzaakt wordt effectief te verminderen. Een goede optie lijkt te zijn om zowel het aantal besmette kippen, als de hoeveelheid campylobacters in de kippenmest en op het kippenvlees aan te pakken. Dat kan door extra aandacht te geven aan de hygiëne op de boerderij, door tijdens de slacht het lekken van besmette mest uit de karkassen te verminderen en door het kippenvlees met bijvoorbeeld melkzuur te wassen. Er valt dan een aanzienlijke gezondheidswinst te behalen. Gegarandeerd vers campylobactervrij vlees is alleen mogelijk als al het vlees doorstraald zou worden. De meest doelmatige maatregelen zijn echter alleen vast te stellen als ook economische en maatschappelijke aspecten worden meegenomen. Hiervoor wordt verwezen naar andere rapporten die in het kader van dit CARMA project zijn verschenen.

Trefwoorden: Kwantitatieve microbiologische risicoschatting; ketenmodel; Beheersingsmaatregelen; Blootsstellingsschatting; Epidemiologie

Abstract

Risk assessment of Campylobacter in the Netherlands via broiler meat and other routes

Each year numerous people get ill due to the *Campylobacter* bacterium. Research within the CARMA project aims to advise the Dutch government on dealing with this problem. This report first describes the possible sources of human exposure to campylobacter in the Netherlands. Next to poultry meat, direct contact with (pet and farm) animals and the consumption of raw and undercooked food are identified as important sources. Broiler meat may be the source of many cases of campylobacteriosis. A mathematical model is built to gain insight in the presence and transmission of campylobacter through the broiler meat production chain, from farm to fork. The model is used to assess the effects of interventions to control campylobacter and to reduce the incidence of campylobacteriosis. It shows that a combined approach is promising: reduction of the prevalence of colonised birds and lowering of the numbers of campylobacters in the faeces and on the broiler meat. This may be achieved by further improvement of farm hygiene, reducing faecal leakage during processing and decontamination of the carcasses with lactate. Implementation of these interventions may result in a considerable public health profit. It is not possible to guarantee fresh campylobacter free broiler meat, unless the meat is irradiated. To select the most effective interventions, economic and social aspects are included in the analysis. This is described in other reports written within the CARMA project.

Keywords: Quantitative Microbiological Risk Assessment; Farm to fork risk model; Control measures; Exposure assessment; Epidemiology

Contents

Summary

Research performed within the CARMA project aims to advise the Dutch government on dealing with the public health burden due to campylobacteriosis. This report first describes the possible sources of human exposure to campylobacter in the Netherlands. For this purpose, results of a laboratory driven case control study is combined with an exposure assessment study. Comparison of these approaches shows a discrepancy in the predicted incidence. Despite some differences in the ranking of sources, not only poultry meat, but also direct contact with (pet and farm) animals and the consumption of raw and undercooked food are identified as important sources by both studies.

Broiler meat may be the source of many cases of campylobacteriosis. A mathematical model is built to gain insight in the presence and transmission of campylobacter through the broiler meat production chain, from farm to fork, including a dose-response relationship. This quantitative microbiological risk assessment model is constructed using the Modular Process Risk Modelling (MPRM) methodology. First, a baseline model describes the 'present' situation in the Netherlands, for chicken breast fillet and a cross-contaminated salad. Parameter estimates of this model are based on the scientific literature and, when data were lacking, on expert judgement. The model includes some novel aspects compared to previously published risk assessments of campylobacter in broiler meat. It explicitly includes variability between flocks and between birds and differentiates between numbers of campylobacters in the faeces and on the carcass. The model dynamics include the basic non-linear dynamics of cross-contamination.

Next, the risk model is used to assess the effects of interventions to control campylobacter and reduce the incidence of campylobacteriosis. A set of interventions is proposed by the risk management in the CARMA project, ranging from the farm to industrial processing and the consumer stage. The effects of these interventions are translated to modified parameter values. Comparison of model outputs (the number of predicted cases) then allows evaluation of the effects of the interventions. It shows that it is not possible to guarantee fresh campylobacter free broiler meat, unless the meat is irradiated. However, some interventions may yield a considerable lower human incidence of campylobacteriosis. A combined approach is most promising: reduction of the prevalence of (flocks of) colonised birds and a decrease of the numbers of campylobacters in the faeces and on the broiler meat. This may be achieved by further improvement of farm hygiene, reducing faecal leakage during processing and decontamination of the carcasses with lactate. An important finding is that interventions aimed at lowering the concentration of campylobacter may be quite effective, despite the fact that campylobacter is not eliminated. To select the most effective interventions, economic and social aspects are included in the analysis. This is described in other reports written within the CARMA project.

1. Introduction

This report is part of the CARMA (Campylobacter Risk Management and Assessment) project, a collaborative project of several Dutch research institutes which aims to advise the Dutch government on possible interventions to reduce the number of cases of campylobacteriosis in the Netherlands. It is a predominantly technical report on the quantitative 'farm to fork' risk model of the broiler chicken production chain as constructed within CARMA, including an analysis of the importance of chicken meat as a route of transmission in comparison with other routes. For details on Campylobacter, campylobacteriosis and the CARMA project we refer to Havelaar (2001) and Havelaar et al. (2005).

Scope

Broiler chickens are generally regarded as one of the main sources of campylobacteriosis. Campylobacter is frequently found in broiler chickens and on broiler chicken meat. Humans can thus be exposed to campylobacter by the consumption of improperly heated chicken meat or other foods which are cross-contaminated with campylobacter during food preparation of an (accompanying) meal with chicken meat.

The relevance of chicken meat as source of Campylobacter infections is explored first. Next, the scope of the 'farm to fork' risk model described in this report is to assess and compare the effects of interventions, aiming to reduce this exposure, all over the broiler chicken meat production chain. Hence, the scope of the model is all Dutch cases of campylobacteriosis originating from the consumption of food contaminated with campylobacter in the Netherlands, originating from broiler chickens. The model excludes human campylobacter infections of Dutch people acquired abroad. In assessing the number of cases without interventions, consumption of broiler chicken meat of non-Dutch origin is included in the analysis, with the assumption that all the meat can be treated alike, independent of country of origin. However, the interventions will be directed at Dutch broilers and broiler meat only. The impact of this complication is discussed elsewhere (Mangen et al. 2005a).

Model demarcation

Due to restrictions in research time and resources, and additional restrictions in knowledge and data availability, the broiler meat risk model has been restricted to one route of exposure only. A detailed analysis of one route only allows the inclusion of details that may have an important impact on the (non-linear) dynamics of the transmission of campylobacter through the 'farm to fork' chain. Finally, the conclusions of this single route are extrapolated to the broader scope as defined above.

Therefore the broiler meat risk model described in chapters 3 and 4 of this report deals with Dutch private home consumers of a salad which is cross-contaminated with campylobacter from chicken breast fillet. It is restricted to meat originating from Dutch processing plants and animals reared in the Netherlands. The food product is chosen because chicken breast

fillet is a raw chicken product which is frequently prepared in Dutch private homes. The presumed route of exposure from chicken breast fillet is cross-contamination, because the fillets are usually cut and cooked. The campylobacters on the fillet are inactivated, but there is a potential for cross-contamination via hands and kitchen equipment. If the cross-contaminated food is consumed raw (like a salad) the risk of exposure is largest.
The model described in this paper starts at the point where broilers enter the processing plant. A preceding model on the dynamics of Campylobacter on the farm is constructed by partners in the CARMA project (Katsma et al. 2005). Their model provides input to our model on flock prevalence and animal prevalence. Also, results from the farm model are taken into account that are associated with the effects of several risk reducing interventions at the farm. The endpoint of the baseline model is the number of cases of campylobacteriosis in a year in the Netherlands, acquired by salad consumption by the route described above.

General approach
Effects of possible interventions are evaluated by first describing the present situation in the Netherlands (defined as the situation in the year 2000 at the start of the project). Next, the effects of separate interventions on this present situation are evaluated. Here, interventions are incorporated as changes in some model parameter values, and effects are generated as model outputs at the end of the chain model. This allows comparison at the same end point of different types of interventions at different points in the farm to fork chain. Also, the effects of combinations of interventions can be studied.
As the aim of the CARMA project is to advise the governmental risk management by the end of the project, the model uses the best knowledge as available at the moment. We apply a scientific methodology and use the available data and knowledge generated by scientific research. However, if the scientific information is insufficient, ambiguous or absent, we use the opinion of available experts as a best estimate. This implies that the result of our assessment reflects the best available knowledge at the time, to serve risk management. Although quantitative, the purpose of the model is not to predict correct numbers expressing levels of exposure to campylobacter and illness rates. The primary objective is to compare the effects of (sets of) interventions, based on the available knowledge.
Additionally, modelling is a good tool to structure the available information and to identify important gaps in data and knowledge. Thus it also generate prioritised research questions that need answers to best improve the advice for risk management.

Context
This report is not the first publication on quantitative risk assessment of Campylobacter in broilers. The model builds further on risk assessments performed in Canada (Fazil et al. 1999), the United Kingdom (Hartnett et al. 2002) and Denmark (Rosenquist et al. 2003) and for WHO/FAO (Anonymous 2001, Anderson et al. 2003). In general, the modelling approach that we apply is more mechanistic than before, and more precisely deals with variability and uncertainty. Also, the model presented in this report is embedded in the CARMA project. It uses input generated elsewhere in the project (Katsma et al. 2005), and gives input to other parts. The final advice to the risk management combines the results

presented here within the results of an analysis of costs (Mangen et al. 2005a) and an analysis of social acceptance of interventions by different groups of stakeholders (Bogaardt 2005). Other routes of exposure, next to chicken meat, are studied by Evers et al. (2004) and Doorduyn et al. (in prep a), as summarized in chapter 2 of this report.

Outline

The main focus of this report is the risk model on campylobacter in broiler meat. In chapter 2 the importance of chicken meat as a source of campylobacteriosis is explored in comparison with other sources, using both an epidemiological approach and a comparative exposure assessment approach. Chapter 3 first describes the methodology applied for the chicken meat risk model. It presents the models constructed for the consecutive stages of the farm to fork chain and the parameter estimates of the baseline model, which represents the present situation in the Netherlands. Then, it describes the baseline scenario and the effects of the selected interventions and a series of alternative scenarios developed to explore the impact of some assumptions and uncertainties in the model. In chapters 4 and 5 modelling results are presented and discussed. Section 5.5 of the discussion particularly deals with uncertainties like those related with the extrapolation of the results to the broader scope of the model. It also gives a list of the ten key simplifying assumptions of the risk assessment, of which the risk management should be aware.

2. Campylobacter transmission via routes other than broiler meat

In this chapter attention will be given to all possible transmission routes for Campylobacter. First, a summary of the setup and results of the epidemiological (so called CaSa) study will be given. Second, the same will be done for the comparative exposure assessment. Finally, the two studies will be compared, discussing similarities and differences.

2.1 Estimation of the relative importance of Campylobacter transmission routes and risk factors based on a laboratory driven case-control study

This chapter is based mainly on two draft papers on risk factors for endemic gastro-intestinal illness due to *Campylobacter jejuni* and *Campylobacter coli*, respectively (Doorduyn et al. in prep a, Doorduyn et al. in prep b) and a report to the ministry of Public Health on risk factors for endemic *C. jejuni,* congress presentations and workshop proceedings.

2.1.1 Introduction and objective

In the Netherlands, hardly any epidemiological data on risk factors for campylobacteriosis are available. Therefore a large case-control study was conducted to investigate risk factors for endemic human campylobacteriosis (and salmonellosis) in the Netherlands, the so-called CaSa-study. The CaSa-study aimed to quantify the contribution of different risk factors in order to provide quantitative data as input for the risk assessment study CARMA. By doing so, it will be possible to predict the efficiency of control and intervention measures and to identify possible new leads for control strategies. In this chapter we present the results of analyses of risk factors associated with endemic campylobacteriosis due to *C. jejuni* and preliminary results for *C. coli* infection.

2.1.2 Study design

Cases

This study was designed as a case-control study and was conducted from April 2002 to April 2003. Cases were culture-confirmed patients with Campylobacter (or Salmonella) infection, identified by the examination of faecal samples submitted to all Regional Public Health Laboratories (RPHL) in the Netherlands. Isolates were sent to the Animal Sciences Group (Lelystad) for confirmation of the species identification by the RPHL.

Controls

Controls (aiming at two per case) were selected from the population registries of 25 municipalities within the service area of the RPHL by frequency matching for age, sex, degree of urbanization and season of the expected numbers of cases.

For the risk factor analysis, only cases and controls that did not travel to foreign countries in the 7 days prior to symptom onset (cases) or completion of the questionnaire (controls) were included.

Questionnaire
The questionnaires for cases and controls included questions regarding food consumption, kitchen hygiene and food processing, contact with animals, occupational exposure, travelling, water recreation activities, recent use of medication (during the previous four weeks) and contact with persons with diarrhoea or vomiting. Cases were questioned about the 7 days prior to symptom onset and controls about the 7 days prior to completion of the questionnaire. Parents were asked to complete questionnaires for young children.

Population covered
The incidence of culture-confirmed campylobacteriosis was calculated using the total number of cases identified from the RPHL divided by the population covered by these laboratories. The routine surveillance of salmonella, based on a long tradition of sending in all first isolates by all RPHL, has repeatedly shown a coverage of about 64% of the Dutch population. Campylobacter surveillance since 1995 has been based on weekly enumeration by all RPHL except one, covering 62% of the regular salmonella surveillance. The CaSa-study allowed for adjustment for underreporting and the time each laboratory participated in the study and estimated that the population coverage for campylobacter was 48%.

Statistical analysis
Standard univariate and multivariate logistic regression was used to estimate odds ratios (OR) and their respective statistical significance and confidence intervals. Because of the design of the study, age, sex and urbanization cannot be studied as risk factors in the univariate and multivariate models and are added to the models as adjusting variables only. Age-stratified analyses are necessary to study age-specific risk factors. Missing values were handled using multiple imputation. This method is recommended to avoid bias in analyses of epidemiological data with missing covariates. The logistic regression results (OR and confidence interval) from five imputed data sets were pooled to obtain a single final result. The population attributable risk (PAR) of each risk factor was calculated based on the multivariate odds ratios as the number of cases attributable to the risk factor divided by the total number of cases. The number of cases attributable to the risk factor was calculated as the total number of cases minus the estimated number of cases if the risk factor was absent, which was estimated by weighing the cases according to their exposure status. Exposed cases were weighed as 1/OR of exposure, non-exposed cases as one. Although each OR is an independent risk in the final multivariate model, going back to the original cases to compute the corresponding PAR causes this PAR to pick up some attributive risk from related covariates. Therefore, summing-up PAR's corresponding to individual independent OR's sums up to a higher value than computed directly for the whole set of risk factors.

2.1.3 Results

Incidence

The overall incidence of laboratory confirmed campylobacteriosis, including travel-related cases, estimated from the CaSa-study was 40.1 per 100,000 person years (table 2.1). For the whole of the Netherlands this means about 6500 cases. This takes estimated coverage and underreporting into account as mentioned in the study design-section. About 10% was admitted to a hospital; 22% was travel-related. With 7% of controls travelling within 7 days of completion of their questionnaire this means a population attributable risk (PAR) of 16% for *C. jejuni* (CI_{95}: 15-17%) and 29% for *C. coli* (26-30%).

Among cases with a job or attending school, about 75% had been absent. The majority of cases, about 89%, concerned infections by *C. jejuni*, about 8% *C. coli* and 2.5% others or unknown species (C. other spp. in table 2.1).

Table 2.1 Campylobacter cases and controls enrolled in the CaSa-study and those responding by returning the questionnaire.

	Controls	*C. jejuni*	*C. coli*	C. other spp.	*C.* spp.
Questionnaires sent	10,250	2833 (89.4%)	256 (8.1%)	80 (2.5%)	3169 (100%)
Incidence / 100,000 person years		35.8	3.2	1.0	40.1
Laboratory confirmed cases		5805	525	164	6494
Questionnaires received:					
including travel	3409	1292	121	33	1446
excluding travel-related cases	3165	1013	82	28	1123
Percentage travelling cases	7%	22%	32%	15%	22%

Non-response analysis

Non-response analysis was based on data on age, sex and urbanization, available for each case and control approached to fill in the questionnaire. No significant differences were found between those who did and did not fill in the questionnaire. This makes it plausible that a selective response did not play a major confounding role in the epidemiological risk analysis.

Risk factor analysis

The results of the risk factor analysis in table 2.2 refers to that performed for endemic infections with *C. jejuni*, 1013/1123, *i.e.* 90% of the Dutch laboratory-confirmed cases. Most risk factors that were significant in the final multivariate model have been previously found. It must be noted that the PAR values in table 2.2 and 2.4 are preliminary. In total, the PAR of the risk factors combined in the final model for *C. jejuni*, add up to 51%. Chicken consumption was shown to be the main identified route of transmission (PAR=23%), but a considerable portion was transmitted by pets. Note however that the 95% confidence interval

for chicken consumption is wide, i.e. 10% - 33%. Quite a large risk was related to the use of anti acid-secretory drugs (9%).
Clearly, next to chicken consumption a range of other risk factors were important with a surprising role of undercooked seafood (PAR=4%). However, traditional risk factors like contact with farm animals, raw milk consumption, water recreation and kitchen hygiene could not be shown to have a significant independent contribution to the risk of infection with *C. jejuni*. Moreover, supposed risk factors as contact with animal faeces and visiting pets were more common in controls than in cases (significant OR<1). The consumption of a whole range of foods was (statistically significant) more common in controls than in cases: meat in paste (croquette, sausage roll), fish (especially regular), hard-boiled egg, dairy products (not raw), salad, fruit, chocolate and nuts. Instead of talking about 'protective' foods it might be worthwhile to analyse the food data by distinguishing a one-sided diet from a varied diet and compute the PAR of this hypothetical life-style related risk factor.

Table 2.2 Risk factors for endemic infections with Campylobacter jejuni in the final multivariate model (preliminary results from Doorduyn et al. (in prep a)).

Risk factors for endemic infections with *Campylobacter jejuni*	Cases N (%)	Controls N (%)	OR final model (95 % CI)	PAR (%) (95% CI)
Chicken	773 (77)	2196 (70)	1.4 (1.1-1.8)	23 (10-33)
Undercooked meat	188 (19)	316 (10)	2.1 (1.7-2.7)	10 (8-12)
Meat prepared at bbq/grill/microwave	292 (29)	626 (20)	1.7 (1.4-2.1)	12 (8-15)
Undercooked seafood	83 (8)	202 (6)	1.7 (1.2-2.4)	4 (2-5)
Eating in a restaurant	459 (46)	1257 (40)	1.3 (1.1-1.6)	11 (4-16)
Ownership of dogs				6 (0-11)
1 dog < 1 yr old	29 (3)	40 (1)	2.3 (1.3-4.0)	
1 dog >= 1 yr old	183 (18)	532 (17)	1.1 (0.9-1.4)	
Several dogs, all >= 1 yr old	49 (5)	85 (3)	1.7 (1.1-2.6)	
Several dogs, at least 1 < 1 yr old	16 (2)	17 (0.6)	2.7 (1.2-5.9)	
Ownership of cats	268 (27)	698 (22)	1.3 (1.1-1.6)	7 (3-10)
Occupational exposure to raw meat				2 (0-2)
Cook / catering industry	20 (2)	23 (1)	2.2 (1.1-4.4)	
Butcher / meat-packing industry	12 (1)	14 (0.5)	2.3 (1.0-5.4)	
Other	9 (1)	23 (1)	1.1 (0.4-2.9)	
Contact persons with symptoms outside the household	120 (12)	328 (11)	1.5 (1.1-2.0)	4 (1-6)
Use of proton pump inhibitors	101 (10)	69 (2)	4.5 (3.1-6.5)	8 (7-9)
Use of H2-antagonists	16 (2)	23 (1)	2.6 (1.3-5.3)	1 (0.4-1)
Total risk factors				51

Preliminary results of the risk analysis of *Campylobacter coli* show some similarities and differences with that of *C. jejuni*. One important difference is the absence of a significant role

of chicken. Remarkable, because both *C. coli* and *C. jejuni* occur in poultry in a proportion of about 30%/70%, respectively. If survival in food and pathogenicity would be the same, a significant PAR should have been found for chicken for *C. coli*. The low number of *C. coli* cases may have caused the OR for chicken consumption to be statistically not significant. However, the role of undercooked meat was significantly higher (PAR= 25%; CI_{95}: 18-29) and that of meat prepared at barbeque, grill or microwave oven seems slightly higher as well (20%). The role of anti acid-secretory drugs is even larger for getting an infection with *C. coli* as for *C. jejuni* (PAR=19%, respectively 9%) Other risk factors for infection with *C. coli* are food bought at a stall (10%); swimming (17%) and game (5%) and tripe (4%). Ownership of cat or dog or a small kitchen dresser, were significant in the univariate analysis only. A 'one-sided diet' comes out as an important risk factor as well for illness due to a *C. coli* infection. Except for the consumption of chicken, it seems as if potential risk factors for *C. coli* appeared more clearly and larger as for *C. jejuni*. Note, that this is true notwithstanding the fact that the number of *C. coli* cases is 1/12 that of *C. jejuni*. This might support the notion of the role of immunity. Exposure to *C. coli* is assumed to be considerably less frequent than for *C. jejuni*, and acquired immunity consequently lower. This may explain why swimming water comes out so clearly as a risk factor for *C. coli* and not for *C. jejuni*. Less immunity to infections with *C. coli* might also explain why anti acid-secretory drugs contributed significantly more to *C. coli* than to *C. jejuni* infections.

2.2 Estimation of the relative importance of Campylobacter transmission routes based on exposure assessment

This chapter is based for the main part on a previous report in Dutch, which was written for the CARMA project (Evers et al. 2004).

2.2.1 Introduction and objective

To attribute human campylobacteriosis to different sources and transmission routes, epidemiological methods have mainly been used (See 2.1). 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. In case of Campylobacter the epidemiological approach suffers from low numbers of observations and the absence of one dominant risk factor. Due to a lack of cases in studies addressing the general population the larger case-control studies are laboratory-driven. These enrolled cases are strongly selected with respect to severity or duration of the disease, which in turn is related to age. Selection may also be involved with respect to genetic susceptibility, general health status, medication (anti acid-secretory drugs) and life style.

An alternative method for source attribution is based on risk assessment techniques. With this method, the relative importance of transmission routes is determined by estimating the human

exposure via each of these routes. This new approach is explored here. By using human exposure to Campylobacter as an endpoint, we assume implicitly that the effect of exposure (described by the dose-response relationship) is independent of the route. This alternative method may improve insight as obtained by the traditional epidemiological approach, and will show gaps of knowledge.

2.2.2 Method

Transmission routes

We considered three categories of transmission routes: consumption of food; direct contact with animals; and water. In more detail:

- Consumption of food (raw or prepared): chicken fillet, chicken other, turkey, pig, cattle, milk, sheep, fish from aquaculture, fish from fisheries, shellfish, crustaceans, vegetables, soft fruit, and firm fruit (19 routes in total);
- Direct contact with animals: pet animals (cat, dog, rabbit and small rodents), farm animals (cattle, pig, poultry, goat and sheep) and city farm (also called petting zoo) animals (9 routes in total);
- Water: swimming in indoor pools, swimming in recreational water, consumption of drinking water (3 routes in total).

Foreign travel was not incorporated. It was known that travelling is associated with increased risk of campylobacteriosis. However, calculations of the exposure due to travelling is not feasible due to the large variation in the contamination of possible reservoirs and in the hygiene behaviour of travellers.

Calculation scheme and output

The output of the calculations is the exposure which is expressed as the mean number of campylobacters ingested per person per day, averaged over the whole Dutch human population. This is calculated per transmission route. The exposure is thus considered at the population level and not per exposure event.

The calculation schemes differ somewhat between categories and transmission routes. One example per transmission route is given below.

For transmission via food consumption, multiply:

- gram food consumed per person per day (population mean);
- fraction contaminated products in retail;
- Campylobacter concentration (number/g) in contaminated products in retail;
- fraction cross-contamination, in case of preparation.

Raw products are consumed raw, i.e. the product is not heated at any point in time between slaughter and consumption. For raw products, all campylobacters are assumed to survive. Prepared products are heated sometime between slaughter and consumption. If prepared, it is assumed that 0% of the campylobacters survive and transmission is then entirely assigned to cross-contamination prior to preparation. So it is assumed that undercooking can be neglected, while we are aware that this is a somewhat uncertain assumption.

For city farms, an example for the direct contact category, multiply:
- number of visitors per day;
- 1/(number of inhabitants in the Netherlands);
- fraction of contaminated animals;
- number of contacts with animals per person per day in these farms;
- probability of contact with faeces given contact with animals;
- gram faeces ingested per faeces-contact;
- Campylobacter concentration (number/g) in contaminated faeces.

We account for the different animal species in city farms by using weighted (according to fraction of total animal population per species) mean values for prevalence and concentration.

For recreational water, an example for the water category, we distinguished two age categories (≤ 12 years and >12 years of age) that differ in visiting frequency and water intake. Multiply:
- fraction of the population in the age category;
- visiting frequency (number of visits per person per day);
- water intake (litre per visit);
- Campylobacter concentration in the water (number per litre).

The result of this multiplication is added for both age categories to arrive at the mean exposure for the whole Dutch population.

Uncertainty

The calculations are done with point estimates for the parameters: estimates of mean values for a whole year for the whole of the Netherlands. In this study we only consider the uncertainty in these point estimates. This excludes variability between persons, time and place (e.g. in amounts consumed and prevalences). In the base scenario, we used PERT distributions (see Vose (2000)) for the uncertainty of the point estimates, described by the most likely, minimum and maximum values. In this study, the most likely value is always taken halfway the minimum and maximum value, which implies it is also the mean and the median value. Data are interpreted as the median value of the mean. The uncertainty of the mean is described on absolute or log scale depending on the specific parameter. This is determined by the nature of the measurements, the research field and the size of the uncertainty. Further, in general the uncertainty is taken larger when less data are available and the size of the uncertainty is taken analogous between categories for a specific parameter. To investigate the effect of the chosen base scenario, two alternative scenarios were evaluated also. These are, first, increased uncertainty ranges (doubled for absolute ranges, multiplied by ten for log ranges) and second, use a uniform distribution instead of a PERT distribution.

Calculations

The calculations were done with Monte Carlo simulation: multiply samples from probability density functions that represent the uncertainty of the mean values of the parameters, according to the calculation schemes above. The calculations were done in @Risk (an Add-

inn of Excel), using 10,000 iterations per simulation. This proved to give satisfactory convergence.

2.2.3 Data

Obtaining data proved to be difficult: much information is lacking. When available, literature or other data were used, but for a part of the parameters, rough estimates not based on data had to be used. The estimated uncertainty, especially of the last mentioned category of parameters, is large. The situation is relatively good for the water transmission routes. Below, the most uncertain parameters are given. Main bottlenecks are, for food routes:

- Campylobacter concentration in food (few studies are available on counts);
- probability of cross-contamination (based on only two modelling studies on Campylobacter and Salmonella on chicken);
- consumption of raw food (the National Food Consumption Surveys are large studies, but in these studies the information on preparation of food is poor);

and, for direct contact with animals:

- contact frequency with animals (rough estimate);
- probability of contact with faeces given contact (rough estimate);
- amount of ingested faeces (rough estimate);
- concentration of Campylobacter in faeces (limited data availability of counts);

The parameters that especially determine the estimated exposure, as found by simple regression analysis of model output as a function of each parameter separately, are the probability of cross-contamination, the consumption of raw food, the probability of contact with faeces given contact and the amount of ingested faeces.

2.2.4 Results

The results for the base scenario are shown in table 2.3 and fig 2.1. The width of the resulting 95% confidence intervals for the endpoint is usually a factor 100 to 1000. This large uncertainty implies that in most cases it is not possible to draw conclusions on differences in exposure between transmission routes. Fig 2.1 shows that this analysis did not yield a limited set of dominant transmission routes.

The top 5 of transmission routes is formed by city farm, chicken other (=non-fillet chicken) raw, milk raw, farm animal – goat and sheep and farm animal - poultry. The direct contact routes show a relatively high exposure, especially city farm and farm animals. Pet animals show a moderate score compared to all other routes. For water routes, only recreational water shows a rather high exposure. Within the food routes, raw products usually show higher exposure than prepared products. The four foods with highest exposure are all raw. Then going further down the exposure list, raw and prepared products alternate, but the six foods with lowest exposure are all prepared products. The two prepared foods with highest exposure are chicken-other and chicken fillet.

The routes with highest exposure are all raw foods and direct contact routes. Only after that we find other types: recreational water and prepared food (chicken-other). The three categories of transmission routes can be compared by summing up the means per category

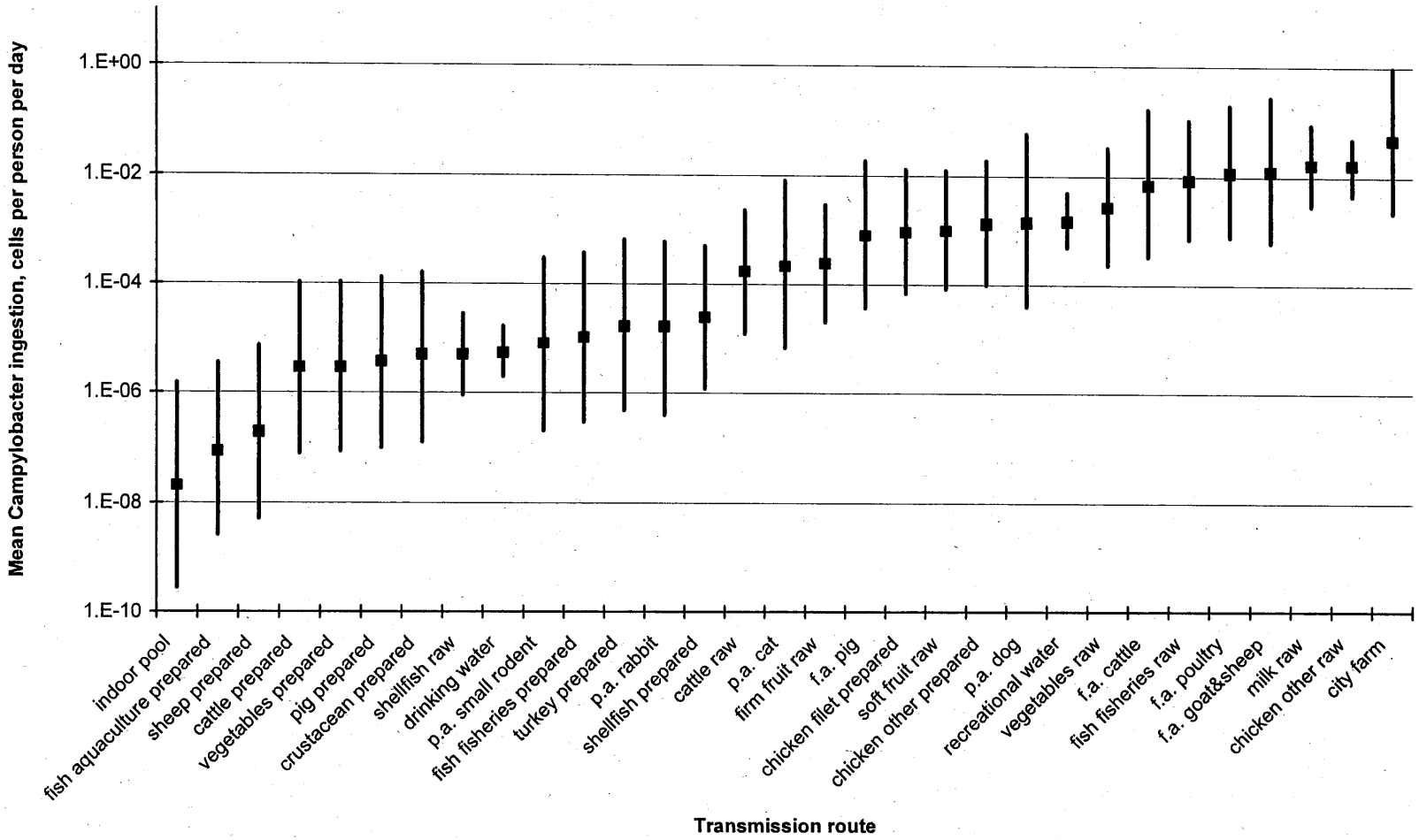

Figure 2.1. Mean ingestion (median and 95% confidence interval) as a function of transmission route, with parameter uncertainties according to the base scenario.
P.a. = pet animal; f.a. = farm animal.

(table 2.3). The result of this will be determined mainly by the routes with highest exposure. This results in the following (campylobacters pppd):

water: 1.48×10^{-3} (= recreational water)
food: 4.96×10^{-2}
direct contact: 8.37×10^{-2}

Table 2.3 Calculated mean ingestion of Campylobacter for the various transmission routes using point estimates for the parameter values.

Transmission route	Mean ingestion (number pppd)
Indoor swimming pool	1.03E-08
Fish aquaculture prepared	9.26E-08
Sheep prepared	1.98E-07
Cattle prepared	2.98E-06
Vegetables prepared	3.03E-06
Pig prepared	3.86E-06
Crustacean prepared	4.97E-06
Shellfish raw	5.16E-06
Drinking water	5.26E-06
Pet animal small rodent	8.70E-06
Fish fisheries prepared	1.08E-05
Pet animal rabbit	1.74E-05
Turkey prepared	1.76E-05
Shellfish prepared	2.53E-05
Cattle raw	1.90E-04
Pet animal cat	2.18E-04
Firm fruit raw	2.53E-04
Farm animal pig	9.16E-04
Chicken fillet prepared	9.45E-04
Soft fruit raw	1.05E-03
Chicken other prepared	1.39E-03
Recreational water	1.48E-03
Pet animal dog	1.50E-03
Vegetables raw	2.82E-03
Farm animal cattle	7.56E-03
Fish fisheries raw	8.86E-03
Farm animal poultry	1.24E-02
Farm animal goat + sheep	1.30E-02
Milk raw	1.67E-02
Chicken other raw	1.73E-02
City farm	4.80E-02

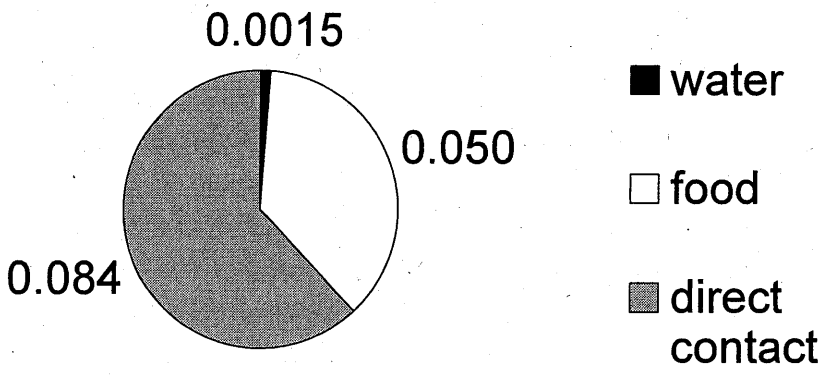

Figure 2.2. Accumulated mean ingestion (no. of campylobacters ingested per person per day) per category of transmission routes.

So exposure by water plays a minor role and exposure by direct contact (approximately 2/3 of total exposure) is more important than by food (about 1/3) (fig 2.2). The sum of all means equals an exposure of 0.135 campylobacters pppd.
The alternative scenarios give little change in what was concluded above. The medians of the mean exposure values are theoretically equal, however the numeric simulation procedure gives minor deviations. The larger uncertainty of the parameters in the alternative scenarios result in even larger confidence intervals for the exposure than found for the base scenario. To illustrate this, in the base scenario 14 routes have confidence intervals that do not overlap with the city farm confidence interval. For the scenarios with increased uncertainty ranges and uniform distributions these numbers are 7 and 5, respectively. So with the alternative scenarios even less can be concluded on differences in exposure between transmission routes. In order to determine which parameters determine most the model output (the exposure), we performed a simple linear regression analysis of model output as a function of each of the parameters. The coefficient of determination (r^2) was used as measure. This shows that for food routes, survival is the most important parameter which implies it is important to know whether a product is consumed raw or prepared. For direct contact routes, the amount of faeces ingested per faeces-contact and somewhat less the probability of contact with faeces given contact and the fraction of the human population that is at risk, are the important parameters. For water routes, the effect of treatment is the most important parameter.

Although the present model is an exposure model, one is tempted to make a simple calculation of the number of human cases of infection based on the estimated exposure, using a dose-response relationship. For this, the Beta-Poisson model was used:

$$P_{inf,\,day} = 1-(1+\mu/\beta)^{-\alpha}$$

with $P_{inf,day}$ the probability of infection per day, μ the dose and α en β parameters. Teunis and Havelaar (2000) give $\alpha = 0.145$ en $\beta = 7.589$. Inserting the value above of 0.135 for μ results

in a value for $P_{inf, day}$ of 2.55 x 10^{-3} pppd. The probability of 1 or more infections per person per year equals:

$$P_{inf, year} = 1 - (1 - P_{inf, day})^{365}$$

This gives $P_{inf, year} = 0.606$. The estimated number of cases of infection with Campylobacter per year for the whole Dutch population according to the exposure model in combination with the dose-response relationship then equals 0.606 * 16 x 10^6 = 9.70 x 10^6. A reasonable estimate is that the number of cases of disease is about equal to 1/3, i.e. 3.2 x 10^6, of the number of cases of infection (Havelaar et al. (2000), footnote page 15). Based on epidemiological data the estimated number of gastro-enteritis cases in the Netherlands per year by Campylobacter is equal to 107,000 (De Wit et al. 2001). So the risk assessment model appears to give a severe overestimation of the number of cases of campylobacteriosis, although it must be kept in mind that the exposure model, the dose-response relationship and the epidemiological estimate are all uncertain. This observation is discussed in 2.3.1.

2.3 Exposure assessment versus epidemiology

Both the exposure assessment and the case-control study have estimated the number of campylobacter cases in the Dutch general population and the relative importance of different transmission routes. It is interesting to discuss the discrepancies of the two approaches on these points. First, the number of campylobacter cases predicted by exposure assessment is much higher than estimated in epidemiological studies in the general population. In fact at the selection level that case-control studies are performed (positive cases from routine laboratory practices) the number of campylobacter cases in the Netherlands is another 17-19 times lower as estimated in the general population. Second, given the difference in estimated cases, it still is interesting to compare the relative importance of transmission routes as estimated by epidemiological analysis (2.1) and exposure estimates (2.2) and attempt to explain the differences.

2.3.1 Number of predicted campylobacter cases

A number of explanations can be given for the difference between the estimated number of symptomatic cases by exposure assessment (3.2 million) and in epidemiological studies in the general population (107,000), see 2.2.4.

Clustering

Exposure is clustered for a part of the transmission routes. 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 others may never do so. If we would take this into account, the non-linear shape of the dose-response relationship, especially the levelling off at high doses, might result in a lower estimate of the total number of cases of infection and illness.

Immunity
Exposure, especially clustering of exposure, may lead to some degree of immunity. This may significantly influence the effect of exposure: (partly) immune persons may have a much lower probability to become infected or ill. Preliminary modelling work on immunity shows that the calculated incidence is much lower when immunity protects against re-infection or illness for a number of years. It also was found that case control research can be strongly disturbed by the occurrence of immunity as well.
Immunity might e.g. play a role in the transmission routes pet animals and farm animals, chicken other raw and raw milk. The last two routes combine a high mean exposure for the whole population with a limited number of consumers. When these 'immunity'-routes are subtracted from the total exposure, then the mean exposure left over is 6.51×10^{-2} campylobacters pppd. The number of campylobacter infection cases in the Netherlands per year according to the model and the dose-response relationship then becomes 5.82×10^{6}, 40 % lower than the previous estimate.

It must be noted that if the first time of an exposure leads to disease severe enough to be enrolled in a laboratory-driven case-control study, the risk factor involved should have been found in such a study. In a general population study that catches only a few cases they may easily be missed. But if the first clustered exposure is more probable to occur in young healthy persons with a high resistance (although not yet immune) it may not lead to disease severe enough to appear as a case in a laboratory-driven case-control study but at the same time would cause some degree of immunity protecting at an older age.

Variable dose instead of mean dose
The output of the exposure model is the mean ingested number of campylobacters per person per day, for the whole Dutch population. This number was used as input for the dose-response relationship. In a more proper way, attention should be given to the variability of the size of the dose that is ingested by people: variability between days, people, place. This variability should in general be described by probability density functions, and samples from these distributions are each by each input for the dose-response relationship. The clustering mentioned above is one aspect of this variability. It is not immediately clear what is the effect of including this variability of the dose on the estimated number of cases of infection.

The dose-response relationship
Dose-response models may overestimate the risk of infection and illness if based on data from outbreaks or from volunteer experiments with a proven pathogenic strain (which is the case in the exposure study of Black et al. (1988). It might well be that a substantial proportion of naturally circulating strains is not or much less pathogenic. Moreover, theoretically, differences in effects of the matrix in which the campylobacters reside, or even genetic host differences may play a role as well. Theoretically this may have a huge influence on the risk estimates.

Exposure estimates
The exposure estimates are generally very uncertain, due to limited data availability. In addition there is no objective theoretical framework to describe this uncertainty. Therefore an overestimation of exposure is possible.

Epidemiological incidence estimate
The epidemiological derived estimate of the incidence of campylobacteriosis in the general population is highly uncertain (20.000-160.000 cases per year in the whole of the Netherlands). Uncertain, but still the upper limit is much smaller than computed straightforward from the exposure estimates. Case definition, focused on acute gastroenteritis, sample storage and culturing may add to an underestimation of the real incidence of all symptomatic cases, including those with mild symptoms or chronic sequelae. An important part of clinical cases of GBS and reactive arthritis caused by campylobacter would not have been identified by the standard case definitions used for a symptomatic (acute) gastro-enteritis and is even often asymptomatic directly after infection.

2.3.2 Relative importance of transmission routes

In this section the relative importance of transmission routes as indicated by the CaSa study and the exposure study will be compared. Attention will be given to differences in the setup of the studies and to similarities and differences in the estimated importance of transmission routes. In the comparison we will mainly concentrate on the *C. jejuni* PARs. In table 2.4 results from both studies are brought into one table. In this table, the group ranking from top to bottom is determined in the first instance by the epidemiological categories with significant PARs and the remaining groups are ranked according to the exposure study.

Aspects that make a comparison difficult
When comparing the results of the epidemiological CaSa study with the exposure model, a number of differences are found between these studies that make a comparison difficult. In general, typical differences in the epidemiological study with the factors considered in the exposure estimation are questions related to food preparation, storing and kitchen hygiene; place of consumption (at home or elsewhere); living conditions; age of pets; profession-related contact with animals, food or infected people; family composition; living conditions and proxies of behaviour and susceptibility as age, sex and socio-economic status. Some aspects in more detail:

- One starting point in the exposure model is that undercooking of food plays a negligible role in transmission. When prepared (heated), all transmission takes place by cross-contamination before preparation. The raw food that is consumed, is food that is left unheated on purpose (e.g. chicken liver, steak tartare). In CaSa, there are categories like 'undercooked meat', 'meat prepared at barbeque, grill, microwave', and 'undercooked seafood'. This makes a comparison difficult.
- In the exposure model, some foods are divided in more categories than were found statistically significant in the CaSa model: e.g. on the one hand 'sheep', 'cattle',

'turkey' and 'pig' in the exposure model and on the other hand 'meat' in the final CaSa model; 'chicken fillet prepared', 'chicken other raw' and 'chicken other prepared' in the exposure model versus 'chicken' in the final CaSa model.
- There are a number of categories that are investigated in the CaSa study and not in the exposure model: game, tripe, eating in a restaurant, food bought at stall, contact with persons with symptoms outside the household, occupational exposure to raw meat (as a cook or as a butcher) and anti-acid secretory drugs (proton pump inhibitors and H_2-antagonists).
- The exposure model considers *C.* spp. As a whole, while in CaSa *C. jejuni* and *C. coli* are distinguished.

Comparing major categories
In the exposure model the categories food, direct contact and water were accumulated and compared as a whole. The conclusion was that only food and direct contact are important; direct contact is more important than food (fig 2.2). The role of water is not clear as well in the CaSa study (*C. jejuni* vs. *C. coli*), but obviously food is more important than direct contact.

Chicken
Chicken is in the CaSa study by far the route with the highest PAR. In the exposure study chicken (or any route) is not much higher than the other routes. It is in second place in this study in the form of 'chicken other raw' and it is also noticeable that 'chicken other prepared' is the prepared food with the highest exposure. If we suggest immunity to play a role, the 'regular' exposure to chicken is not expected to be as high in the CaSa study as it is. In fact several other case-control studies show chicken eating at home even to be 'protective'. It is relevant to note that chicken is not a statistically significant risk factor for a *C. coli* infection although *C. coli* and *C. jejuni* occur in a proportion of 30/70 in chicken. It may be that *C. coli* does not survive as well as *C. jejuni*. Moreover, we suggested above that the lower exposition in general to *C. coli* would make the role of immunity for *C. coli* less important than for *C. jejuni*. One suggestion might be that imported chicken meat poses a higher risk for infection, e.g. as no 'regular' strains are involved. However we should realise that almost everybody eats chicken, so that with a low OR of 1.4 the PAR is still considerable, but with a large confidence interval. One reason that an OR of 1.4 was found significant is that the CaSa study is one of the largest case-control studies ever on campylobacter.

Non chicken meat
The consumption of meat excluding chicken (i.e. cattle, sheep, turkey, pig) plays a minor role according to the exposure model. This agrees with the not significant PAR for 'meat, not chicken'. The high PAR values found for barbecue/grill/microwave and undercooked meat contradict the assumption of the exposure study that transmission through undercooking can be neglected and/or the implicit assumption (as no separate route barbecue is distinguished) that the probability of cross-contamination with barbecuing is not higher than with other food preparation methods.

Direct contact

The importance of direct contact with dogs and cats and the minor importance of direct contact with other pets (e.g. rabbits, small rodents) was found in both studies. However, although in the exposure study direct contact via city farms and farm animals (goat & sheep, poultry, cattle and to a lesser extent pig) are among the most important routes, these routes are not significant in the final multivariate model in the CaSa study. In the multivariate model risk factors are combined that have an independent contribution to the risk of infection. For example, 80% of the enrolled infected farmers (and those among the controls) had cats and/or dogs. As ownership of cats and dogs is also a risk factor for non-farmers, the unique risk of farmers with respect to farm animals resolves in the multivariate model, but is univariately significant. Hence the epidemiological association with ownership of cats and dogs may very well be an overestimation of the direct causal relationship. It may be a proxy of a behaviour that involves a more frequent environmental contact as well. Indeed within the CaSa study in 90 instances Campylobacter was found in both the patient and in the faeces of their pet but in only 1 case the strains were genetically (AFLP) identical (preliminary results CaSa-study). To clarify this point it is necessary to do specific stratified analyses. Contact on city farms, were not asked for specifically in CaSa but were part of a question on 'contact with animals outside the household'. Here also, ownership of cats and dogs may be a disturbing factor and further stratified analysis might be necessary.

Seafood

In the exposure model, 'fish, fisheries raw' (= herring) was important, whereas other fish categories were unimportant. In the CaSa study, the (partly similar) category 'undercooked seafood (fish, shellfish/crustacean)' was important, and regular fish consumption was 'protective'.

Raw milk

In the exposure study, raw milk is no. 3 on the list, whereas it is not significant in the CaSa study. Raw milk outbreaks are especially related to young children. This clearly indicates that it is an important factor, but age-related development of immunity may play a role. Being focused on sporadic infections, the CaSa study does not indicate a significant contribution. Both immunity and lifestyle factors related to regular raw milk consumption might play a role. But then it must be assumed that a large part of these people developed immunity without first becoming a symptomatic case severe enough to end up in the laboratory surveillance.

Vegetables and fruit

In the exposure study, raw vegetables were among the higher exposures and soft and firm fruit showed a moderate exposure. These routes are protective in the CaSa study. A 'protective' role is also found for nuts, chocolate, dairy products, and fish. It must be noted that this large group of food products with a negative PAR can also be interpreted as a varied 'healthy' diet, as opposed to a one-sided diet hypothetically being a risk factor as a life-style

factor. Prepared vegetables play a minor role in the exposure study and are not included in the CaSa study.

Water

In the exposure study, swimming in recreational water was a moderately important transmission route. It was not significant for *C. jejuni* in the CaSa study, but a clear contribution was found for *C. coli*. In this case immunity might play a role. The exposure to *C. coli* can be considered as rare compared to *C. jejuni* and immunity might consequently be higher for the latter microorganism. A moderate exposure may then lead to an infection with *C. coli* but not with *C. jejuni*. The other transmission routes related to water (indoor pools, drinking water) play a minor role in both studies.

Concluding remarks

It is known (especially from food consumption surveys) that the poor reproducibility in filling in questionnaires may strongly influence PAR estimates. If this bias is random, the relationship of the risk factors questioned with the outcome (disease) is weakened and OR values change to 1 and hence in an absolute sense, lowers the corresponding PAR. It also may influence the ranking and statistical significance of risk factors, especially if differences in accuracy of reporting between risk factors are considerable.

Due to the considerable uncertainties and the confounding effects of e.g. clustering of exposure and immunity, the use of exposure modelling for source attribution of campylobacteriosis is limited. The results of case-control studies are likewise confounded. Crucial is the notion that exposure modelling works at the bottom of the surveillance pyramid, whereas case-control studies focus on a subgroup of infected cases that in the case of CaSa are strongly selected with respect to severity. In this selection genetic susceptibility, general health, medication (anti acid-secretory drugs) and life-style are probably not similar to that for the average case in the general population. They may be more at risk to become symptomatically infected even at a low level of exposure. On the other end, mild or asymptomatic infection in response to a high level of exposure (without being partly immune) may occur in some professions that at the beginning of the career select young healthy persons that become (partly) immune afterwards. In the general population regular low exposure may lead to asymptomatic infection and the development of (partial) immunity protective for incidents of high exposure. Serology studies in the general population in Wisconsin (Belongia et al. 2003) and preliminary results of a similar study on *Campylobacter jejuni*-IgG in the Netherlands suggest that 2-3 million people are infected in such a way that an IgG response is induced. This estimate is much closer to the 5.8-9.7 million cases with the exposure model and emphasizes the role of immunity in explaining the gap between exposure and epidemiological estimates.

Further understanding of the impact of these phenomena on risks of illness and infection is of critical importance for reliable attribution of 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.

Table 2.4 Calculated mean ingestion of Campylobacter spp. (Left) and epidemiologically measured significant population attributable risks (PARs) of C. jejuni and C. coli (Right: preliminary results), for the Netherlands.
A negative PAR would be protective. Rk = original ranking in exposure study; ns = not significant.

Transmission Route	Ingestion (no. pppd)	Rk	Category	PAR(%) *C. jejuni*	PAR(%) *C. coli*
Chicken other raw	1.73E-02	2	Chicken	23%	ns
Chicken other prep.	1.39E-03	11			
Chicken fillet prep.	9.45E-04	13			
Cattle raw	1.90E-04	17	Meat: bbq/grill/microwave	12%	20%
Turkey prepared	1.76E-05	19	Undercooked meat	10%	25%
Pig prepared	3.86E-06	26	'Meat', not chicken	ns	ns
Cattle prepared	2.98E-06	28	Tripe	ns	4%
Sheep prepared	1.98E-07	29	Pork/sausages, at home	ns	(-%?)
			Game	Ns	5%
			Eating in a restaurant	11%	ns
			Food bought at stall	Ns	10%
			Use of anti acid-secretory drugs	9%	19%
Pet animal: dog	1.50E-03	9	Ownership cat(s)	7%	ns
P.a. cat	2.18E-04	16	Ownership dog(s)	6%	ns
P.a. rabbit	1.74E-05	20	Ownership rabbit/ rodent	ns	ns
P.a. small rodent	8.70E-06	22			
			Contact symptomatic persons (outside household)	4%	ns
			Occupat. exposure raw meat	2%	ns
Fish fisheries raw	8.86E-03	6	Undercooked seafood (fish, shellfish/crustacean)	4%	ns
Shellfish prep.	2.53E-05	18			
Fish fisheries prep.	1.08E-05	21			
Shellfish raw	5.16E-06	24	'Fish'	(-%?)	(-%?)
Crustacean prep.	4.97E-06	25			
Fish aqua prep.	9.26E-08	30			
City farm	4.80E-02	1	City farms	ns	ns
Milk raw	1.67E-02	3	Raw milk	ns	(-%?)
F.a. goat + sheep	1.30E-02	4	Contact farm animals	ns	ns
F.a. poultry	1.24E-02	5			
F.a. cattle	7.56E-03	7			
Farm animal: pig	9.16E-04	14			
Vegetables raw	2.82E-03	8	Raw vegetables	(-%?)	(-%?)
Vegetables prep.	3.03E-06	27			
Recreational water	1.48E-03	10	Recreational water	Ns	17%
Indoor pool	1.03E-08	31			
Soft fruit raw	1.05E-03	12	Fruit	(-%?)	ns
Firm fruit raw	2.53E-04	15			
Drinking water	5.26E-06	23	Drinking water	-----	ns

3. Risk Model

3.1 Methodology

3.1.1 Principle

The risk model for Campylobacter in broiler chicken meat constructed for the CARMA project simulates the transmission of Campylobacter through the 'farm to fork' chain and assesses the consequences of human exposure. It follows the changes in the prevalence (frequency of units contaminated with campylobacter) and numbers of campylobacter in contaminated units from stage to stage over the chain. Here, the 'unit' is the potentially contaminated animal or food item, for example the carcass, the fillet or the bird exterior. At the stage of the 'fork', the model describes exposure as the prevalence of ingestion of a contaminated meal and the variability distribution of ingested numbers of campylobacters (doses). A dose-response model then predicts the frequency of infection and illness in the Dutch population in a year.

For the 'farm to fork' exposure modelling we apply the 'Modular Process Risk Modelling' methodology (MPRM) (Nauta 2001, Nauta 2002, Lindqvist et al. 2002, Nauta 2005). In this methodology, all relevant processes are described in terms of basic processes (bacterial processes growth and inactivation; food handling processes partitioning, mixing, cross-contamination and removal). This approach gives a clear structure of the food chain, and allows us to include the basic dynamics of the processes. The level of detail of these models depends on the relevance of the process step for the dynamics, the availability of data, and the specific risk management questions regarding this process step as considered in the analysis. In MPRM the first step is to consider the basic processes to model, and then to obtain the appropriate data. Within the basic process models non-linear effects that are considered important in the transmission dynamics are incorporated. Such effects can usually not be found from studying the data alone, but may be crucial when the effects of risk mitigation strategies are analysed with the model.

3.1.2 Uncertainty and variabilities

The constructed 'farm to fork' risk model is a stochastic quantitative microbiological risk assessment model. We use Monte Carlo simulation to incorporate the effects of uncertainty and variability in the analysis. For extensive discussion on this issue we refer to for example Vose (2000) and Nauta (2000). In the context of this report it is important to explain the various levels of uncertainty and variability that are dealt with in this study.

First, there is variability between birds within a flock. Quite often not the whole flock of birds is colonized, and the animal prevalence (the percentage of colonized birds) in a flock has a value between 0 and 100% (see also Katsma et al. (2005)). Moreover, also the level of campylobacter contamination on the birds' exteriors and the concentration of campylobacter

in the gut will vary between birds in the flock. Such variability can be described by a probability distribution with one or a few parameters (e.g. a lognormal distribution).
Next, there is a variability between flocks reared and slaughtered in the Netherlands. Not only will some flocks contain colonized birds and some flocks none (i.e. the between-flock prevalence lies between 0 and 100%), also the animal prevalence and the distribution of levels of campylobacter between birds in a flock will vary. Hence, to describe this variability, we need additional probability distributions of for example the animal prevalence and the means of the distributions describing the variability between birds.
Third, there is uncertainty. This uncertainty represents our lack of knowledge due to scarcity of data, imprecise methods of measurement, inadequate representativity of data, etc. Like variability, this uncertainty is often represented by probability distributions. A probability distribution may describe the uncertainty about the true value of a parameter, and also the uncertainty about the mean of a distribution describing variability.
As mixing uncertainty and variability may strongly affect the outcome of a risk assessment (see for an example Nauta (2000)), separation of these is important. For every distribution used in the risk model it should therefore be explicitly clear what it represents. This is not only the case for variability and uncertainty, but also for variability at different levels, like per bird or per flock.
It is not always possible to adequately describe the uncertainty in a probability distribution. If no or hardly any data are available, and even experts find it difficult to make an estimate, one may only have a 'best guess' or a 'wild guess' on hand. In such a case one can decide that the uncertainty is too indeterminate to be described with a probability distribution. An alternative is then to explore the impact of the uncertainty about this parameter by doing separate alternative simulation runs with different values of this parameter in so called 'what-if' scenarios and compare the model outputs. The same procedure can be applied to simplifying assumptions in the risk model.
With variability at two levels and additional uncertainty, a 'farm to fork' risk model can easily become extremely complex. This was the case for the model developed for this study. Instead of a second order Monte Carlo, our analysis became third order and almost intractable. In the final analysis we therefore choose to leave out the uncertainty as a quantitative factor. Our approach was to first define a baseline model with most likely values for all parameters, including those describing the probability distributions for variability between birds in a flocks and variability between flocks. Next, in a set of alternative scenarios, we evaluate the impact of the uncertainties in the model parameters and the model input.

3.1.3 Interventions

The objective of the model is to evaluate and compare the effects of interventions to reduce the public health risks associated with campylobacter in broiler meat. This is done by comparing the baseline model results with results of model runs where the interventions are implemented in the model. For that purpose, the interventions proposed for evaluation by the

risk management represented in the steering committee of the CARMA project have been translated to an effect on model parameters, based on literature and/or expert opinion.
Each separate intervention has been evaluated for its effect on the baseline result.
Additionally, uncertainty bounds have been defined for (some of the) intervention effects on model parameters, to explore the uncertainty about the effect on the change in the incidence of campylobacteriosis predicted by the model with 'what-if' scenarios.

3.1.4 Data sources

In the selection of data used in the risk model, we gave priority to data published in the scientific peer reviewed international literature, describing the year round situation in the Netherlands in the base year 2000. As these data were hardly ever available, we compromised on this by either taking data from other (recent) years, taking data from other (European, Western, industrialized) countries, or taking Dutch data that were not published in the peer reviewed literature. In case of absence of any data from a reliable source, we based our parameter estimates on expert opinion. For industrial processing a formal expert judgement study was performed (Van der Fels-Klerx et al. 2005), for other parts parameter estimates were based on less formal expert estimates of parameter values.
Note that the choice for using expert judgement as a data source was not only governed by availability of poultry processing data, but also by the suitability of these data to be used in the mechanistic non-linear model applied here. In our modelling approach, applying the proper mechanistics in the risk model is considered to be a crucial factor in predicting the effects of interventions. If published data are inadequate to fulfil the data needs of the mechanistic model, (formal) expert judgement is preferred above processing data. The latter can then be used for model validation.

3.1.5 Model implementation

The risk model is constructed using @Risk 4.5 (Palisade, Newfield), an add on on Microsoft Excel. For practical reasons the model is split up in two spreadsheet models, one for processing (including deboning and cutting) and one for storage, consumer food handling and dose-response (infection and illness) .
In the processing model, one iteration simulates the fate of 500 birds from one flock processed in line. This group of 500 is large enough to represent a broiler flock, and small enough to allow spreadsheet model calculations. Model input informs about the animal prevalence in that flock, and the distribution of numbers of campylobacters on the exterior of the birds and distribution of the concentration of campylobacter in the faeces of the birds. The result gives information on within-flock variability. At the endpoint it yields the number of campylobacters on 500 chicken breast fillets from that flock. To get a representative sample, a set of 5000 iterations then simulates 5000 flocks. If the differences in input and parameter values of these 5000 iterations describe between-flock variability only, the results should be interpreted as such too. Likewise, if the differences in input and parameter values of these 5000 iterations describe uncertainty only, the results should also be interpreted in terms of uncertainty (about one typical flock). If the differences in input and parameter values of these

5000 iterations describe both, this should be taken into account in the interpretation of the results.
The consumer model starts with 5000 distributions of numbers of campylobacter per fillet, from 5000 flocks. It samples fillets from these distributions, which are independently stored, handled, and prepared together with salad. Dose- response predicts the number of cases from the resulting doses. Here, data on consumption frequencies and meal sizes in the Netherlands are taken into account. As a standard, the consumer model is run for 100.000 iterations, sampling 20 fillets from the distribution of each flock, for 5000 flocks.

3.1.6 Extrapolation: from model objective to project scope

The risk model calculates the expected number of cases of campylobacteriosis resulting from the consumption of salad prepared after handling raw chicken breast fillet. The exact numeric result is not as important as the relative effects of interventions, as we are aware of the many uncertainties and model simplifications that were necessary for the risk assessment. This implies that for the final conclusions we make a linear extrapolation to all chicken related food consumption leading to campylobacteriosis in the Netherlands. To us, this was the preferable approach, given a lack of simple alternative approaches and the constraints in data and research time. Thus, it is assumed that the effects of proposed intervention are relatively the same in our restricted model and for the whole scope of the project. These effects are used in the economic analyses (Mangen et al. 2005a).

3.2 Model description

3.2.1 Overview

Table 3.1. Overview of units modelled in the stages of the risk model.
'broiler flock' (with quotation marks) refers to groups of products derived from one broiler flock.

	input unit	*output unit*
Farm	broiler flock	broiler flock
Processing	broiler flock	'broiler flock'
	carcass	carcass
Cutting	'broiler flock'	'broiler flock'
	carcass	fillet
Storage	fillet	fillet
Consumer preparation	fillet	salad
Ingestion / Dose-response	salad	probability of illness

The food pathway described by the risk model extends from the entrance of a flock of live broilers into the processing plant, to consumption of salad in a meal prepared together with raw chicken breast fillet. The pathway is split up in some major consecutive stages: (1) Processing (slaughter and industrial processing of the carcass); (2) Cutting (of the carcass to a skinned chicken breast fillet); (3) Storage (before and at retail, and by the consumer); (4) Consumer handling (of the fillet, and the salad prepared along with it) and (5) Ingestion (potentially of a dose of Campylobacter. A dose-response relation is used to predict the consequential probability of illness).

It is important to realize how the units modelled changes over the food pathway. This is summarized in table 3.1. As in the MPRM framework, prevalences are defined as the percentage (fraction) of contaminated units and numbers of campylobacter are numbers (integers) per unit.

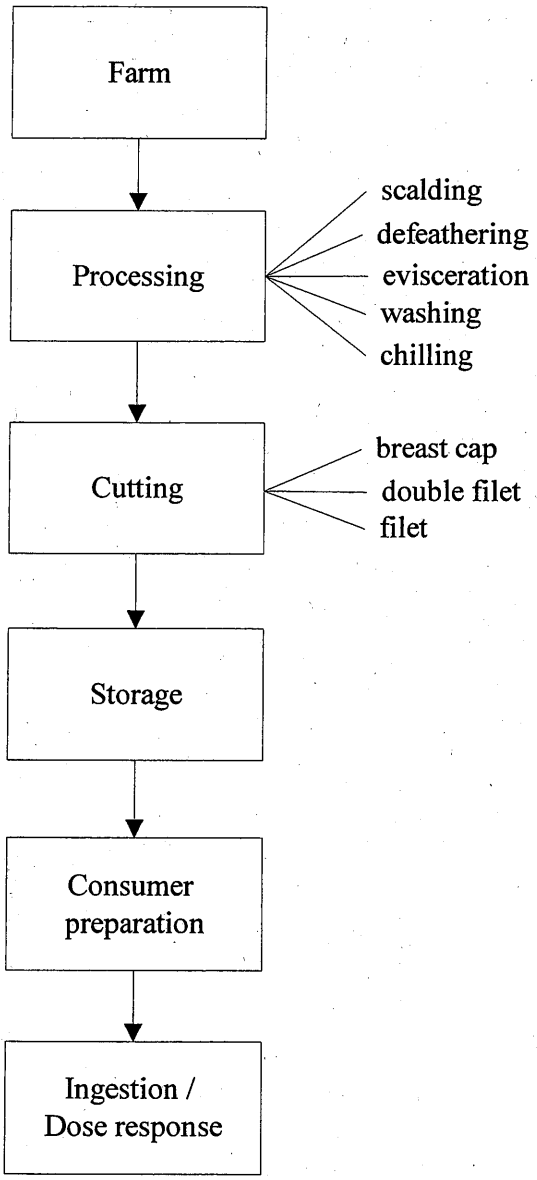

Figure 3.1 Food pathway of the risk model.

3.2.2 Processing

In the fully automated poultry processing plant it has become impossible to isolate individual carcasses from other carcasses or from equipment, employees and other materials essential for processing, resulting in possible cross-contamination at all stages of the process (Hafez 1999). Scalding, defeathering and evisceration, in which faeces contaminated with campylobacter may leak from the carcasses, are supposed to be the most critical points for cross-contamination during processing (Anderson et al. 2003, Hafez 1999, Kist 2002). At the scalding stage a proportion of campylobacters is washed off the carcass, resulting in contaminated scald water and subsequent cross-contamination to the next carcasses in line (Anderson et al. 2003, Hafez 1999). During defeathering a proportion of organisms is washed off or removed with the feathers, but a number of organisms is added via cross-contamination (Anderson et al. 2003, Kist 2002). According to Anderson et al. (2003) and Kist (2002) evisceration leads to contamination of a carcass via cross-contamination, but might also result in a proportional reduction. During washing and chilling the bacterial counts on carcasses decrease. The final number of organisms that are on any carcass is a result of the initial contamination and the effect of all stages of processing (Anderson et al. 2003).

As a processing model we apply the model of Nauta et al. (2005). The consecutive processing stages scalding, defeathering, evisceration, washing and chilling are each described by applying the same basic processing model. In the Netherlands low scalding (with water temperatures 50-52°C) and air chilling are applied for the production of fresh meat like chicken breast fillets. In MPRM terminology, this basic model combines the basic processes inactivation, removal and cross-contamination, and thus incorporates the basic mechanisms that may be relevant during processing. The model formulation is given below. For details and discussion on the process and the model dynamics, we refer to Nauta et al. (2005).

Consider a line of broiler chickens processed. At each of the consecutive processing stages, a carcass i entering stage S is contaminated with $N_{ext,S-1}(i)$ cfu (colony forming units) campylobacter on the exterior (skin and, if present, feathers). Here, if S is the scalding stage, S-1 refers to the entrance of the processing plant, if S is defeathering, S-1 refers to the values after scalding, etc. Next, at stage S, $N_{fec,S}(i)$ cfu leak from carcass i with the faeces (interior), where $N_{fec,S}(i)$ is the product of $w_{fec,S}(i)$, the mass of leaking faeces (in grams) and $C_{fec}(i)$, the concentration in cfu campylobacter per gram faeces. There is a direct environment of the carcass that gets contaminated, either by campylobacter from the exterior, or by campylobacter in faeces leaking from the carcass. This environment can be anything that gets contaminated by contact with the passing animals and from which campylobacter may be transferred back to the carcass, e.g., water, equipment, hands, air. It holds $N_{env,S}(i)$ cfu campylobacter after the passage of carcass i (which, with this conceptual definition, cannot be measured).

In every processing stage S cross-contamination, inactivation and removal (per carcass) may occur as presented in fig 3.2, be it that faecal leakage is no longer relevant after removal of the intestines during evisceration.

The parameters and variables of the poultry processing model are listed in tables 3.2 and 3.3. This yields the following model equations per stage S and carcass i:

$$\begin{cases} N_{ext,S}(i) = (1-a_{ext,S})(1-c_{ext,S})N_{ext,S-1}(i) + b_{env,S}N_{env,S}(i-1) + (1-a_{fec,S})N_{fec,S}(i) \\ N_{env,S}(i) = a_{ext,S}N_{ext,S-1}(i) + (1-b_{env,S})(1-c_{env,S})N_{env,S}(i-1) + a_{fec,S}N_{fec,S}(i) \end{cases} \quad (1)$$

With $N_{ext,S}$ (i) the number of campylobacters on carcass i at the end of stage S (and thus at the start of stage S+1), $N_{env,S}$ (i) the number of campylobacters in the environment after passage of carcass i (and thus prior to the entering carcass i+1) in stage S, and $N_{fec,S}$ (i) the number of campylobacters in the leaking faeces of carcass i at stage S, that is the product the concentration of campylobacter in the faeces and the mass of leaking faeces, $w_{fec,S}(i) \times C_{fec}(i)$. Processing stages are linked as the output of stage S-1, $N_{ext,S-1}(i)$, is the input of stage S.
As model input we need a value for the initial number of campylobacters in the environment per processing stage, $N_{env,S}$ (0) and (variability) distributions of $N_{ext,\,input}$ and C_{fec} per carcass entering the processing plant. In applying the distribution of C_{fec} the animal prevalence p_{anim}, the percentage of animals in a flock colonized by campylobacter, is incorporated. We assume

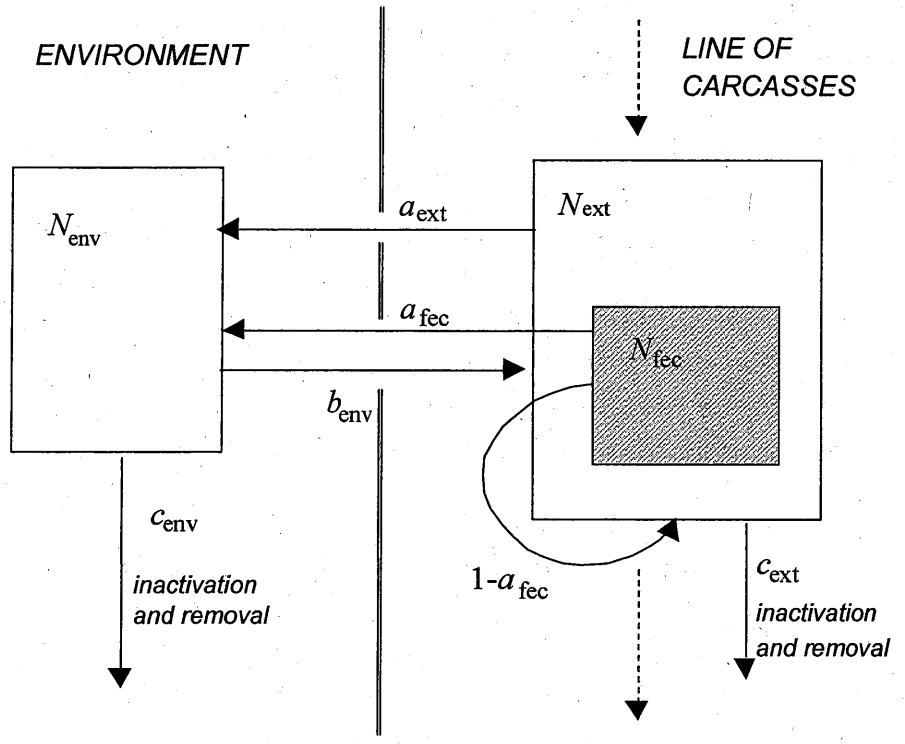

Figure 3.2. Diagram of the basic poultry processing model.
At any stage during processing, consecutive carcasses (at the right) pass an environment (at the left), as indicated by dashed arrows. The passing carcass holds N_{ext} campylobacters on its exterior and N_{fec} = $C_{fec} \times w_{fec}$ campylobacters leak from its intestines. Cross-contamination may occur when campylobacters from the exterior and (if appropriate) in the leaking faeces are transferred to this environment and backwards from the environment to the exterior of passing carcasses. Next, campylobacters on the carcass and in the environment may be inactivated or removed. See main text for explanation of the parameters.

Table 3.2 Model parameters.
Subscript S indicates that the parameter values differ per processing stage S. Per processing stage all parameters have fixed values.

$a_{ext,S}$	probability per cfu campylobacter on the exterior (skin and feathers) to move from the carcass exterior to the environment.
$b_{env,S}$	probability per cfu campylobacter in the environment to move from the environment to the carcass exterior.
$a_{fec,S}$	probability per cfu campylobacter in the leaking faeces to move to the environment. (With corresponding probability 1-$a_{fec,S}$ per cfu to move from the interior to the exterior of the carcass directly.)
$c_{env,S}$	probability of inactivation or removal per cfu campylobacter in the environment which is not transferred to the carcass exterior.
$c_{ext,,S}$	probability of inactivation or removal per cfu campylobacter on the carcass exterior which is not transferred to the environment.
$p_{fec,S}$	probability of faecal leakage per carcass.
p_{anim}	fraction of the animals in a flock colonized by campylobacter.

Table 3.3 Model variables.
Variables have different values per carcass and are sampled in Monte Carlo simulation or calculated with eq. (1). Subscript S indicates processing stage S.

$m_S(i)$	amount of faeces (gram) that leaks from carcass *i,* given faecal leakage; sampled from a lognormal distribution with mean $\mu_{m,S}$ and standard deviation $\sigma_{m,S}$.
$w_{fec,S}(i)$	amount of faeces (gram) that leaks from carcass *i:* with probability $p_{fec,S}$ $w_{fec,S}(i) = 0$, else $w_{fec,S}(i) = m_S(i)$
$C_{fec}(i)$	campylobacter concentration in the faeces of carcass *i*, identical per carcass *i* for all stages (cfu/g faeces). Model input, by default sampled from a lognormal distribution defined as 10^Normal(μ_C, σ_C)
$N_{fec,S}(i)$	number of campylobacters in the leaking faeces from carcass *i:* $N_{fec,S}(i) = w_{fec,S}(i) \times C_{fec}(i)$.
$N_{ext,S}(i)$	number of campylobacters on the exterior after processing of carcass *i*. $N_{ext,input}(i)$ is model input, by default sampled from a lognormal distribution defined as 10^Normal(μ_N, σ_N), rounded to integer. For the other stages $N_{ext,S}(i)$ is calculated with eq. (1) and rounded to integer.
$N_{env,S}(i)$	number of campylobacters in the environment after processing of carcass *i*. Calculated with eq. (1). By default, $N_{env,S}(0)$ is set to the expected value (see Nauta et al (2005)).

that all carcasses are contaminated on their exterior due to cross-contamination during rearing and transport, be it that the level is lower with lower animal prevalence. Next, it is assumed here that the input distributions of $N_{ext,input}$ and C_{fec} (per contaminated animal) are lognormal. As the value of $N_{ext,input}$ (cfu) should be an integer, samples of the lognormal distribution for this variable are rounded to integer.
Faeces may leak from the carcass intestines at the stages scalding, defeathering and

evisceration. One of the variables for this faecal leakage is the mass of faeces leaking, $w_{fec,S}(i)$. It does not seem realistic to assume a fixed value for this variable as leakage will differ substantially per processed carcass, and this variability can be taken into account. First, there may be no leakage at all: $w_{fec,S}(i)= 0$ with probability $1-p_{fec,S}$. With probability $p_{fec,S}$, leakage occurs with a variable amount $w_{fec,S}(i)=m_S(i)$ per carcass i. This $m_S(i)$ is described by a lognormal distribution with mean μ_m and standard deviation σ_m. $p_{fec,S}$ has a fixed value. The expected value of w_{fec} is $E(w_{fec}) = p_{fec}\ \mu_m$.
This chicken processing model is implemented as a Monte Carlo simulation model. In this model, levels on individual carcasses are followed throughout the process as numbers (cfu) per carcass. Input values for $N_{ext,input}$, C_{fec} and $w_{fec,S}$ are sampled per simulated carcass, from the given distributions. Values of $N_{ext,S}(i)$ and $N_{env,S}(i)$ are calculated with eq. (1) and rounded to integers. The output of the poultry processing model includes the distribution of numbers of campylobacters on the exterior of carcasses from the processed flock ($N_{ext,chilling}$).

Processing model parameter estimates
The processing model requires parameter estimates that could not be based on data reported in the scientific literature. Although some data on changes in levels of Campylobacter in chicken processing lines are available (e.g. Oosterom et al. 1983, Izat et al. 1988, Berrang and Dickens 2000), these data could not be transformed in a format applicable in this study. Also, the representativity of these data for the Netherlands in 2000 is uncertain. The data are however used in other published international campylobacter risk assessments (Hartnett et al. 2002, Rosenquist et al. 2003, Anonymous 2001, Anderson et al. 2003), as discussed in section 5.6.1.
We therefore performed a formal expert judgement study, as published by Cooke et al. (2004) and Van der Fels-Klerx et al. (2005). In this study, twelve Dutch and one British expert(s) were consulted and weighted on the basis of their scores on a set of query variables. The study resulted in a set of interdependent uncertainty distributions of the model parameters for each stage of processing. An overview of these uncertainty distributions is given in the Appendix.
In our baseline risk model we apply the median values of these distributions as default estimates of all model parameters. These medians, as presented in table 3.14, are considered to best represent the central values of the distributions due to the skewness of many of the distributions. Note that the values given are the result of the structured analysis of the expert judgement data (Cooke et al. 2004, Van der Fels-Klerx et al. 2005). By this analysis, the parameter combinations found yield the best fit with the expert estimates and their attending uncertainty, and hence the results offer the best reflection of the expert opinion. Comparison of the values of individual parameter at different processing stages may give counterintuitive results, e.g. for a_{ext} at evisceration (a_{ext}=0.46) and washing (a_{ext}=0.31). This should however be regarded in combination with the estimates of the other parameters estimates and the resulting prediction for the total effect of the processing stages considered. These predictions agree with the expert opinions.
The estimates for the leaking faeces parameters p_{fec} and $m_{s\mu}$ followed directly from answers of the experts to queries regarding the probability of faecal leakage and the amounts leaking,

and are not integrated in the probablistic inversion. As we were not able to estimate $m_{s\sigma}$ from the expert data, and its values appears to be largely irrelevant, it is set at a low value, 0.001.

3.2.3 Cutting

At the cutting stage chilled carcasses are deboned and portioned. First, breast caps are cut from the carcass, and then the (double) fillets are cut from these, and skins are removed. Most of this is done by equipment, but people's handwork may be involved too. Here we define a fillet as a single fillet, i.e. half the fillet originating from one carcass.
Count data on the effects of cutting on the numbers of Campylobacter on the chicken products are scarce. Berrang et al. (2001) counted campylobacters and other bacteria on broilers after defeathering, after evisceration and at retail in the USA. They studied the effect of skin removal by looking at products with and without skin. Whereas no campylobacters were found on the naked meat after defeathering, they could be recovered after evisceration. The level on the meat was only about 1 log lower than on the skin, which suggests substantial cross-contamination due to damaged skins. At retail there was no difference between the level of contamination on the naked meat and on the skin. They concluded that '*broiler parts purchased at retail outlets are not microbiologically different because of presence or absence of skin. However, removal of skin from a partially processed broiler carcass may be useful in lowering the level of contamination carried forward in the plant.*'
An important difference in chicken processing between the United States and the Netherlands is the application of water chilling instead of air chilling. This may for a large part explain the cross-contamination leading to the equal levels found on and below the skin. The water applied at chilling may leak through the (damaged) skin, carrying along the bacteria.
In a Belgian study Uyttendaele et al. (1999) found campylobacter in 71 out of 183 samples with skin (38.8%) and in 45 out of 180 (25%) in samples without skin (detection limit > 1 cfu/100 cm^2 or 25 g), which is a significant difference ($P<0.05$). This contradicts the finding of Berrang et al. that levels on and beneath the skin are the same. A difference that may be explained by the difference in chilling methodology.
As these literature data can be assumed to be not representative for the Dutch situation (Berrang et al.), or are insufficiently detailed (Uyttendaele et al.) we base our parameter estimates on expert opinion. As research time was limited at this stage of the project, we were not able to perform a formal expert study on this topic, as we did for the processing stage. Only one expert (J. Obdam, head Research and Development, Plukon Poultry, Wezep, the Netherlands) was interviewed. (His estimates are to be considered as rough guesses, kindly provided at our request. The authors of this report are responsible for applying these estimates in this study.)
The available information on the dynamics of transmission of campylobacter during this process is limited. We therefore apply a simple model, based on the insights gained from modelling the previous stages.
The relevant basic MPRM processes are partitioning (the fillet is cut from the carcass) and cross-contamination/removal (from skin to fillet, from equipment to fillet, etc.). For these, we apply two separate models:

Partitioning

Cutting the breast cap from the carcass is a partitioning process, as described in Nauta (2005). The number of campylobacter from the breast cap *i*, $N_{ext,bc}(i)$, will depend on the number on the carcass after chilling $N_{ext,chill}(i)$ and the probability for each campylobacter on the carcass to reside on the breast cap, p_{cut}. So:

$$N_{ext,\,bc}(i) \sim \text{Bin}(N_{ext,\,chill}(i), p_{cut}),$$

or with variable, beta distributed p_{cut}:

$$N_{ext,bc}(i) \sim \text{BetaBin}(N_{ext,\,chill}(i), \alpha_1, \alpha_2)$$

(where ~ indicates 'is a sample from'.) The value or the distribution of p_{cut} will depend on the relative weight of the breast cap or the (double) fillet, but also on the relative surface (as campylobacters are situated on the surface) and the clustering of campylobacters on this surface.

The relative weight of a double fillet compared to a carcass after chilling, is on average 24% (J. Obdam (pers. comm.), see also the Dutch 'Handboek voor pluimveehouderij', *in press*.) However, this is not the relative surface. If a carcass is considered to be a sphere, and the breast cap a slice from this sphere, some basic mathematics shows that the relative surface is about 32%. However, incorporating the fact that a carcass is not a sphere (but has legs etc.) this percentage will probably be lower again.

We therefore assume that a distribution with a mean value 24% is not a bad choice, assuming it may lay somewhere between 10% (a guess) and 32%. The variability between breast caps may be very large, certainly if the probable contagious distribution of campylobacters over the carcass is taken into account.

As a best guess we apply a Beta(1, 3.15) distribution for p_{cut}, as illustrated in fig 3.3 . As alternatives in the uncertainty analysis we take different values of α_1 (default $\alpha_1 = 1$) and the mean $\mu = 24\%$.

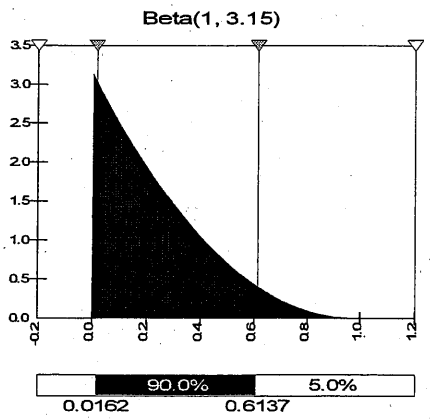

Figure 3.3 Variability distribution Beta (1, 3.15) applied for the probability for each cfu campylobacter to end up on the breast cap.

The mean of this distribution is $\mu = 24\%$. 90% of the samples from this distribution falls within the range of 2% and 61%.

Cross-contamination / removal

The fillet is cut from the breast cap and the skin is removed. As campylobacters are supposed to be absent or rare on the skinless meat prior to slaughter, they are tranferred to the meat by cross-contamination. This can either be by passing through tears in the skin, along with water leaking under the skin during processing, or during the cutting process. Here, based on discussions with experts, we assume the latter to be the dominant route.

Ideally, we would like to apply the same methdology as for the processing model. However, as data are very limited we choose to use a simplified version of this model.

The number on a double fillet is $N_{ext,df}(i)$. It is a function of the number on the breast cap and the expected number in the environment (equipment, hands, etc, as in the processing model) $E(N_{env,df})$. As discussed by Nauta et al. (2005), eq. (1) can be simplified for N_{ext}, assuming that the model dynamics approach an equilibrium state in which the number of campylobacters in the environment is unaltered, so that $\Delta N_{env} = 0$:

$$N_{ext,df}(i) = a\, N_{ext,bc} + \beta\, E(N_{env,df})$$

Here, a and β are parameters. Parameter $a = (1-a_{ext,df})/(1-c_{ext,df})$ describes the effect of inactivation and removal and $\beta = b_{env,df}$ describes the effect of cross-contamination. Nauta et al. (2005) have shown that from the processing model (eq. (1).) it can be derived that, by the lack of faecal contamination, $E(N_{env})$ is a function of the expected value of N_{ext}, as:

$$E(N_{env,S}) = \frac{a_{ext} E(N_{ext,S-1})}{b_{env} + c_{env} - b_{env} c_{env}}$$

so with $\varphi = \beta\, a_{ext}/(b_{env}+c_{env}-b_{env}c_{env})$

$$N_{ext,\,df}(i) = a\, N_{ext,bc} + \varphi\, E(N_{ext,bc})$$

and

$$E(N_{ext,\,df}(i)) = (a + \varphi)\, E(N_{ext,\,bc}).$$

Here, $a + \varphi$ is the expected fraction of campylobacters transmitted from breast cap to double fillet. Furthermore, a is the contribution of the breast cap i that the double fillet is cut from, and φ is the contribution of the environment in the total number of campylobacters on the fillet after cutting. By a lack of data, these parameters can be estimated based on expert opinion.

Finally, to get the number on the single fillet we get:

$$N_{ext,\,f}(i) = 0.5\; N_{ext,df}(i)$$

The expected fraction transmitted from breast cap to double fillet, a + φ is estimated to be about 0.01 to 0.02, based on unpublished data on other bacteria (J. Obdam, pers. comm.) According to Berrang et al. (2001) it lies close to 1, but as explained above we do not consider this representative for the Dutch situation. Furthermore, *a* is the relative contribution of breast cap *i* itself, and φ the relative contribution of the environment to the total campylobacter contamination of the fillet after cutting. The expert guesses that about 17% of the contamination originated from the carcass itself, so a/(a+φ) =0.17.
Defining $\pi = a+\varphi = 0.0158$ (i.e. $10^{-1.8}$, an intermediate value between 0.01 and 0.02) and $z = a/(a+\varphi) = 0.17$, applying $a = \pi z$ en $\varphi = \pi (1-z)$, estimates for *a* and φ can be calculated as $a=0.0027$ and $\varphi = 0.0132$
The uncertainty in these parameter estimates is large and is explored in the section of alternative scenarios. For log π we assume that the uncertainty ranges from about -1.3 to -2.3, that is 0.5 log above and below the most likely estimate. For *z* we consider a range from 0.1 to 0.25. Variability in the estimates is not included in the model.

3.2.4 Storage

After cutting the fillets are stored and transported. In modelling terms that means that for some time they experience a variable temperature profile. Typically, the potential inactivation of Campylobacter during this process should be modelled by a secondary survival model. However, information and data are lacking to apply such a model here.
During storage and transport, the temperature is kept constant somewhere between 1 and 7°C, but this may vary between cutting plant, transport, retail, consumer transport, and consumer refrigerator. The storage time may vary, especially due to the variability in consumer behaviour. The variety of time temperature profiles encountered is presumably large and unknown.
The survival dynamics of Campylobacter on chicken meat is not well known either. There is however clear information that survival is not 100%. In a study on Campylobacter survival, Curtis et al. (1995) found that on raw chicken breast 10^6 cfu/g Campylobacter can not be recovered after 24, 13 and 6 days at resp. 2, 10 en 20°C, with a 'detection limit' of 50 cfu/g, i.e. a decrease by 0.18, 0.33 en 0.72 $\log_{10}$ units per day. Chan et al. (2001) tested strains from poultry and clinical human strains at 4°C. In broth, fitting their data shows that variability in inactivation between strains is best described by an Exponential(0.25) $\log_{10}$ units/day distribution, for clinical strains exponential(0.17), for poultry exponential(0.34). These are results comparable with Curtis et al. (1995). For the impact of refrigeration Hartnett (2001) applies a D-value of 2.88 days as found by Koidis and Doyle (1983) brucella broth without sodium bisulphite at 4°C. That is 0.35 log units per day. With decreased oxygen levels (as in prepacked fillets), inactivation slows down. However, we have little information on the oxygen levels during storage and transport.
For the CARMA risk model we apply information from data gathered for the CARMA project (Jacobs-Reitsma et al. in prep.). Fillets from six different flocks processed in the summer of 2004 in the Netherlands were sampled and Campylobacters were counted directly after cutting. Fillets of the same flock were individually stored in plastic bags for a week at

4 °C, and then counted. Lognormal distributions were fitted through the count data applying Maximum Likelihood Estimation (MLE) methodology. With this method count data yielding information of upper and lower limits only can be included in the analysis, and estimates of both the mean and the variance of the numbers counted are obtained. Results are shown table 3.4. There is a decrease between 0.1 and 1.9 logs in counts due to storage, with a mean value of 0.9. This is not in contrast with the inactivation data from literature, if some tailing effect of inactivation is taken into account.
In the risk model we apply a simple inactivation model

$$log\ (N_{ext,\ fs}(i)) = \log\ (N_{ext,\ f}\ (i)) - r_{storage}\ .$$

For this model we need an estimate of decrease in survival after storage, $r_{storage}$. This is assumed to be variable, described by a BetaPert distribution incorporating the variability in survival during storage as found in the experiments of Jacobs-Reitsma mentioned above:

$$r_{storage} \sim \text{BetaPert}(0.1, 0.9, 2.1)$$

(Here the maximum value is taken somewhat larger to account for the small sample size)

Table 3.4 Results of campylobacter counts on chicken breast fillets (Jacobs-Reitsma et al. in prep.) for six flocks processed in the summer of 2004 in the Netherlands.
Presented are the mean and sd (between brackets) of the normal distribution fitted through the log counts. Stored fillets are stored for one week at 4°C. Count data for flock 6 were not obtained.

flock	1	2	3	4	5	7
sample size	20	20	10	20	20	20
fillet	3.53 (0.29)	4.01 (0.48)	2.96 (0.26)	3.23 (0.35)	3.23 (0.48)	2.92 (0.68)
stored fillet	3.42 (0.39)	2.75 (0.44)	2.19 (0.31)	2.47 (0.33)	1.33 (0.55)	2.55 (0.49)

3.2.5 Consumer preparation

For consumer preparation we apply the model for cross-contamination during food preparation as developed by Mylius et al. (submitted). It describes cross-contamination from raw chicken meat to hands, cutting board, water tap and salad, based on several studies on cross-contamination of bacteria in a kitchen environment. It is assumed that the chicken meat is well cooked, and consequently all campylobacter on the meat is killed off. Cross-contamination to the salad, which is consumed raw, is therefore considered to be the only relevant route of cross-contamination. This can be either from raw chicken meat via the hand to the salad or from raw meat via the cutting board to the salad.
The model holds transfer coefficients $t_{X,Y}$, expressing the probability for each cfu Campylobacter to be transferred from X to Y during the handling X and Y. Transfer from and to Chicken meat (C), Hands (H), Cutting Board (B) and Salad (S) are considered. Transfer coefficients $t_{H,H}$, $t_{B,B}$ and $t_{S,S}$ express the probability of survival per cfu Campylobacter during hand washing, board washing and salad washing.

The number of campylobacters ending up in the salad for meal of table-companions *i* ($N_{salad}(i)$) will then be:

$$N_{salad}(i) = (t_{C,H} \times t_{H,H} \times t_{H,S} + t_{C,B} \times t_{B,B} \times t_{B,S}) t_{S,S} N_{ext,fs}(i).$$

Next to transfer probabilities of campylobacters, it is important to take frequencies of type of handling into account. That is: the effect of hand washing, board washing or salad washing is only relevant if they are actually washed. If not, the transfer coefficient will have value 1. Also, the chicken fillet should be cut before the salad for cross-contamination to occur and it should be done on the same (side of the) cutting board for cross-contamination via the cutting board to occur.
Data on the frequencies of these handlings are collected from the literature (Mylius et al. submitted). We also applied data derived from statements of the controls in the case control study on Campylobacter and Salmonella conducted in the Netherlands during 2002-2003, as given in table 3.5. (Doorduyn et al. (in prep a), see chapter 2.1). As these statements may suffer some optimistic bias as found when statements and actual observations are compared (see Redmond and Griffith (2003)), the data indicating proper behaviour are interpreted as somewhat too optimistic. The frequency of hand washing is rounded off to 80%: for hand washing between cutting meat and vegetables the sum of 'always' and 0.5 × 'usually' is 86%, but other studies give lower estimates (Worsfold and Griffith 1997, Redmond and Griffith 2003). For board handling the 3% using the same board side is rounded up to 5%. (For comparison: for this value Kusumaningrum et al. (2004) take the average of five international data sources, 26%, so rounding up seems appropriate.) The effect of turning around the board is assessed to be the same as washing, as the probability of transfer may be larger than when a different board is used. Estimates for the frequencies of each type of food handling are given in table 3.6.

Table 3.5. Statements on food handling behaviour of n = 3409 Dutch controls of the case control study performed by Doorduyn et al. (in prep a).

Hand washing between cutting meat and vegetables			Hand washing before cooking			Board handling		
	n	*%*		*n*	*%*		*n*	*%*
always	2624	77	always	2088	61	use different board	1081	34
usually	519	15	usually	992	29	turn around board	218	7
sometimes	137	4	sometimes	232	7	use same board side	103	3
rarely	41	1	rarely	41	1	wash board	1809	56
never	25	1	never	21	1			
no answer	63	2	no answer	35	1			

The values of the transfer coefficients are given in table 3.7. The variability in the transfer coefficients is incorporated in the model. For this purpose, we apply probability distributions reported in the literature (Kusumaningrum et al. 2004), or Beta distributions fitted through the raw data presented in the literature (Montville et al. 2001, Chen et al. 2001) or Pert distributions with minimum, most likely and maximum values reported (Cogan et al. 2002, Smith et al. 2003). For each model iteration in the consumer model (see 3.1.5) values of transfer coefficients are sampled from these distributions (see table 3.7). For washing transfer coefficients, the frequencies listed in table 3.6 have to be taken into account.

- For hand washing, with probability f_{hw} : $t_{H,H} \sim$ Beta(0.24, 6.67), else $t_{H,H} = 1$;
- For cutting board washing there are three scenarios as illustrated in fig 3.4. With probability $f_{nsb} \times f_{bw}$ the board is washed (or turned around): $t_{B,B} \sim$ BetaPert(1,4.5,7), and with probability $f_{nsb} \times (1\text{-}f_{bw})$ another board is used so $t_{B,B} = 0$. (see fig 3.4). With probability 1-f_{nsb} the same cutting board is used and not washed, so $t_{B,B} = 1$;
- For salad washing, with probability f_{sw} : $t_{S,S} \sim$ BetaPert(0,0.4,1), else $t_{S,S} = 1$.

Table 3.6. Frequencies in which food handling activities are assumed to be performed in the risk model.

action		frequency	reference
Hand washing	f_{hw}	80%	Doorduyn et al. (in prep a)
Cutting board washing	f_{bw}	65%	Doorduyn et al. (in prep a)
Salad washing	f_{sw}	60%	Worsfold and Griffith (1997)
Not same board side used	f_{nsb}	95%	Doorduyn et al. (in prep a)
Chicken cut before salad	f_{cf}	50%	guess, no data

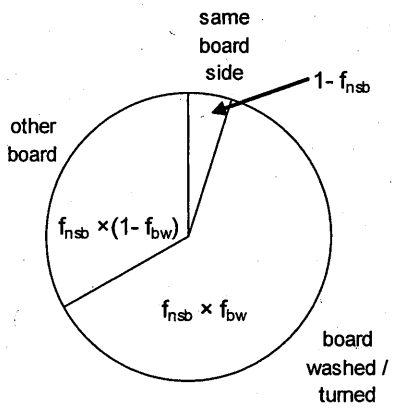

Figure 3.4 Frequencies of board handling as used in the model.

Table 3.7. The mean transfer probabilities per cfu campylobacter and wash-off effects associated with different food handling activities.
In the risk models variability of these probabilities is sampled from the indicated distributions.

transfer / wash off		mean value	variability distribution	reference
Chicken to hand	$t_{C,H}$	0.0415	Beta(1.78, 41.1)	Montville et al. (2001)
Chicken to cutting board	$t_{C,B}$	0.0125	10^Normal(0.098,0.606) %	Kusumaningrum et al. (2004)
Hand to salad	$t_{H,S}$	0.207	Beta(0.6,2.3)	Montville et al. (2001)
Cutting board to salad	$t_{B,S}$	0.343	10^Normal(1,535, 0.32) %	Kusumaningrum et al. (2004)
Hand washing	$t_{H,H}$	0.0347	Beta(0.24, 6.67)	Chen et al. (2001)
Cutting board washing	$t_{B,B}$	0.0000464	BetaPert(1,4.5,7) log reduction	Cogan et al. (2002)
Salad washing	$t_{S,S}$	0.367	BetaPert(0,0.4,1) log reduction	Smith et al. (2003)

3.2.6 Exposure

So far, the risk model assesses the number of Campylobacter in a salad prepared together with chicken breast fillet from a chicken from a contaminated flock, in a private kitchen. This salad will quite often not be consumed by one person, but will be eaten by table-companions joining the meal.

To estimate the distribution of exposures (that is the numbers of campylobacters expressed as cfu ingested), we need data on the consumption of chicken breast fillet together with a salad in the Netherlands. Relevant data are the amounts of chicken meat and salad eaten, the frequency of chicken breast fillet with salad meals and the number of table-companions per meal. For this purpose we apply data from the third Dutch National Food Consumption Surveillance (VCP) (Kistemaker et al. 1998). As one of the dose-response models applied (see section 3.2.7) differentiates between young (14 years and younger) and adults (15 and older), we treat these categories separately.

The data used are presented in tables 3.8 and 3.9. In 2000 the Dutch population size was 15.86 million people, of whom 2.74 million between 1 and 14 years of age. (We exclude 0 years of age due to their presumed deviant consumption pattern). Using the data in table 3.8, it is easy to see that this implies that it is expected that in a year about 9 million meals with chicken breast fillet and salad are eaten by the Dutch population of 14 years and younger, and about 76 million by the 15+ group.

Table 3.8 The number of persons eating one (or more) meals with chicken breast fillet and salad in a two day period, in a sample of 6250 persons in the Netherlands (1178 14- and 5072 15+).
In total 92 joined meals were consumed by 174 people. The corrected numbers $k_{j,v}^*$ are used for sampling as explained in the main text.

table-companions	young (14-)	adult (15+)	all ages	corrected for number of fillets	
v	$k_{y,v}$	$k_{a,v}$	$k_{tot,v}$	$k_{y,v}^*$	$k_{a,v}^*$
1	0	41	41	0	41
2	3	63	66	3	95.29
3	6	18	24	8.55	40.84
4	11	17	28	20.9	51.43
5	2	13	15	4.75	49.16
total	22	152	174		

Table 3.9. Consumed quantities of fillet and salad by the Dutch consumers (Kistemaker et al. 1998.)

consumed quantities (g)					percentiles		
		mean	sd	5%	50%	95%	n
14- fillet	($w_{con,y}$)	75.7	38.5	31.5	68.5	148.5	22
14- salad		84.0	65.6	29.4	75.0	178.6	22
15+ fillet	($w_{con,a}$)	121.5	55.9	38.0	105.0	225.0	161
15+ salad		121.0	96.9	15.0	100.0	312.0	161

With more table-companions, more fillets will be prepared along with a larger salad. This complicates calculations. With an average weight of fillets of about 160 g., it can be seen from table 3.9 (and a more robust analysis of the data, not shown) that there is no simple relationship between the number of fillets and the number of table-companions. Also, the contamination status of different fillets applied in one meal (i.e. whether they are contaminated or not) may be different, and the level of contamination may be different too. This problem is solved by a simplified approach, justified by a lack of adequate data and the fact that it is impossible to account for all the variability in which meals consisting of chicken breast fillet and salad can be accomplished.
Assuming the salad is split up equally between the table-companions, the number of campylobacters ingested will be a sample from a binomial distribution with parameters N_{salad} and probability $1/v$, and v the number of table-companions, for both the young and the adults.
In principle, the number of table-companions is a sample from the frequency distribution given in table 3.8. However, this distribution has to be adapted for the number of fillets prepared along with the salad. This number is estimated to be:

$$n_{fillets}(v, j) = MAX(1, v \times w_{con,j} / w_{fillet})$$

for age class j, and number of table-companions v. (Note that n_{fillet} is a number ≥ 1 and need not be an integer.) Parameter w_{con} is the mean in table 3.9 and w_{fillet} is the estimated average weight of a chicken breast fillet, 160 g.
We simply regard the consequence of one contaminated fillet per salad only, assuming that the contamination of a salad after cutting x fillets is x times as large as with a fillet. We then have to adjust the frequency of the number of table-companions as applied in sampling by this factor:

$$k_{j,v}^{*} = n_{fillets}(v, j) \times k_{j,v}$$

Then for each age class j:

$$v \sim \text{Discrete}(v, k_{j,v}^{*})$$

and

$$N_{consumed,j} \sim \text{Binomial}(N_{salad}, 1/v)$$

which yields the ingested dose.
Here Discrete is a so-called discrete distribution as applied in @Risk and for example described by Vose (2000). Here it means that each v is sampled with probability $k_{j,v}^{*}$.

3.2.7 Ingestion and Dose-response

In the final stage, we aim to predict the probability of illness as a consequence of the consumption of a salad prepared together with a chicken breast fillet. For this purpose, we have to combine the exposure assessment, resulting from the risk model so far, with a dose-response relationship and information on consumption patterns in the Netherlands.
The most frequently used dose-response relationship for Campylobacter is the Beta Poisson model for probability of infection (Medema et al. 1996, Teunis et al. 1999) based on the data of a volunteer study of Black et al. (1988). This Beta Poisson model is a good approximation of the hypergeometric dose-response model (Teunis and Havelaar 2000).
This model states that p_1, the probability of infection by one ingested Campylobacter is variable, as described by a Beta Distribution:

$$p_1 \sim \text{Beta}(\alpha, \beta)$$

The probability of infection due to the ingestion of n Campylobacters is then:

$$P_{inf}(n) = 1-(1-p_1)^n$$

According to Teunis and Havelaar (2000) $\alpha = 0.145$ and $\beta = 7.59$. Hence, the expected value of p_1 is 0.019 implying a 2% probability of being infected after ingestion of a single living Campylobacter cell.
The data of Black et al. (1988) also include information on the probability of illness given infection, for the volunteers in their study. The implications of this information are disputable. Teunis et al. (1999) derive a dose dependent hazard function for this probability:

$$P_{\text{ill}|\text{ inf}}(D) = 1-(1+\eta/D)^{-r}$$

with D the mean dose and η and r shape parameters. Best fitting values for η and r are $\eta = 0.048$, $r = 4.40 \cdot 10^7$. Surprisingly, the resulting dose-response relationship for illness is decreasing for higher doses. (Teunis et al. 1999). Physiologically, this decrease is not well understood, reason to assume it may be an artefact of the data set and the statistical analysis. As a simpler, equally valid model for the probability of illness given infection, it is therefore assumed that

$$P_{\text{ill}|\text{ inf}} = 0.33$$

based on the fact that, in the study of Black et al (1988) a total of 29 people got sick out of 89 individuals that were infected. (Havelaar et al. 2000, Anonymous 2001).
The dose-response model for illness now becomes:

$$P_{\text{ill}}(n) = P_{\text{inf}}(n) \times P_{\text{ill}|\text{ inf}}(n)$$

Recently, Teunis et al. (2005) published a reconsideration of this dose-response model, based on two (remarkably similar) outbreaks (one in the UK (Evans et al. 1996) and one in the Netherlands (Van den Brandhof et al. 2003)) of campylobacteriosis in groups of school children who drank raw milk at a farm visit. Although the ingested doses of Campylobacter were not known in these outbreaks, the relative amounts of milk consumed could be retrieved. The combination of these data with the data of Black et al. (1988) yielded new estimates for the parameters of the dose-response model of Campylobacter, and different estimates for a 'sensitive' population (like young school children) and others (like healthy volunteers) .
In the CARMA project we translate these two populations to 'children aged below 15 (sensitive) and 'adults (15+)' (others). The resulting most likely estimates for the model parameters according to Teunis et al. (2005) are:

adults: $\alpha_a = 0.024$, $\beta_a = 0.011$ (Teunis et al. 2005)
$\eta_a = 0.048$, $r_a = 4.40 \cdot 10^7$ (Teunis et al. 1999)
children: $\alpha_c = 0.024$, $\beta_c = 0.011$ (Teunis et al. 2005)
$\eta_c = 3.63\ 10^{-9}$, $r_c = 2.44 \cdot 10^8$ (Teunis et al. 2005)

Here, the parameters for the probability of infection are identical for adults and children, now with an expected value for p_1 of 0.67, that is 67% probability of infection after ingestion of one living Campylobacter cell. The difference in the probability of illness results from a difference in the hazard functions describing the probability of illness given infection.
As illustrated in fig 3.5, with these new most likely values, the probability of illness as a consequence of low doses increases dramatically. This is a consequence of the steep inclination of the response curves resulting from the two outbreaks. At the moment, the acceptability of this updated model within the scientific community is not yet clear.
In the CARMA risk model we apply the 'Classic' model, based on Black et al. (1988), with $P_{ill|inf} = 0.33$, as the default model. The main reason for this is that this model is now generally accepted by the scientific community. The updated model for children and adults, based on Teunis et al. (2005), (the pink line and the brown line in fig 3.5) are explored as alternatives. Furthermore, the dose-response model is linked with the exposure model by putting $n = N_{consumed}$.

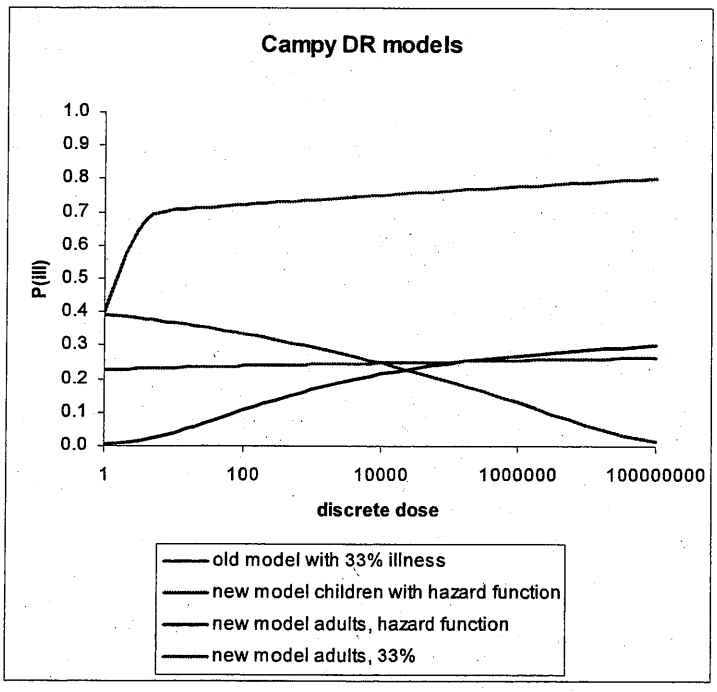

Figure 3.5. Comparison of most likely dose-response curves as currently considered.
The probability of illness is plotted as a function of the discrete ingested dose, n (so the line should be regarded as a series of connected dots). Note the difference in shapes of the curves.
Blue line: 'Classic' model of Teunis and Havelaar (2000) with $P_{ill|inf} = 0.33$. Pink line: Model for sensitives (children), with a hazard function for the probability of illness given infection. Red line: Model for adults, with a hazard function for the probability of illness given infection. Brown line: Model for adults with $P_{ill|inf} = 0.33$. This model more or less implies that $P_{ill} = 0.25$, irrespective of the dose (given, of course, a dose of at least 1). As a baseline we apply the 'Classic' represented by the blue line.

3.2.8 Overview of the risk model

For overview of the risk model, table 3.10 summarizes the chain of models applied that link the number of campylobacters on the exterior of the carcass and the meat product at each stage. For a complete description of the models, see the sections above.
As explained in section 3.1.5. the model is programmed as two spreadsheets using @Risk software as an add on to Microsoft Excel. The first spreadsheet covers the processing model including the cutting stage. The second spreadsheet uses the output of the first: the distributions of $N_{ext,\ cutting}$ per flock, for 5000 flocks. The model covers storage, consumer food handling and dose-response.

Table 3.10. Overview of the models applied for each of the stages of the risk model.
For explanations see the main text.

stage	output	equation	unit
scalding	$N_{ext,\ scald}$	eq. (1)	carcass
defeathering	$N_{ext,\ def}$	eq. (1)	carcass
evisceration	$N_{ext,\ evis}$	eq. (1)	carcass
washing	$N_{ext,\ wash}$	eq. (1)	carcass
chilling	$N_{ext,\ chill}$	eq. (1)	carcass
cutting (1)	$N_{ext,\ bc}$	$\sim$ BetaBin($N_{ext,\ chill}(i)$,α, β)	breast cap
cutting (2)	$N_{ext,\ f}$	$= 0.5(\ a\ N_{ext,bc}(i) + \varphi\ E(N_{ext,bc}))$	(single) fillet
storage	$N_{ext,\ fs}$	$=10^{-r\_storage}\ N_{ext,\ f}(i)$.	(single) fillet
consumer prep	N_{salad}	$= (t_{C,H} \times t_{H,H} \times t_{H,S} + t_{C,B} \times t_{B,B} \times t_{B,S})$ $t_{S,S}\ N_{ext,\ fs}(i)$	salad (table-companions)
exposure	$N_{consumed}$	$\sim$ Binomial(N_{salad}, $1/v$)	meal
response	P_{ill}	$P_{ill}(n) = 1-(1-p_0)^{N\_consumed} \times P_{ill\mid inf}(N_{consumed})$	meal

3.3 Parameter estimates baseline model

The baseline model describes the most likely situation for chicken processing by a large industrial processing plant in the Netherlands in the year 2000. It includes variability between flocks and between birds, carcasses and fillets. Uncertainties are evaluated with the analysis of alternative scenarios.
As model input for the basic model we first need a value for the flock prevalence and a distribution describing the animal prevalences in flocks. These are provided by the farm model (Katsma et al. 2005). Next, we need distributions for the concentration of campylobacter in the faeces $C_{fec,\ input}$ and the numbers of campylobacter on the carcass exteriors $N_{ext,input}$. For the last two we need two types of distributions: the distributions in the flocks and the distribution between flocks. These distributions are to be derived from data.

3.3.1 Flock and animal prevalence

The flock prevalence and animal prevalences at slaughter are provided by the CARMA farm model (Katsma et al. 2005). It is found that the flock prevalence is 44.4%. This is larger than the prevalence found in surveillance studies (Van Pelt and Valkenburg (2001), see also Bouwknegt et al. (2004)), because in these studies flocks with low animal prevalence may not be found positive when the sample sizes are too small. The distribution of animal prevalences is illustrated in fig 3.6. It shows that, as an outcome of the farm model, the animal prevalence is always <1. Of the 44.4% infected flocks, 21% has an animal prevalence <5% and 49% has a prevalence >98%. The large percentage of low prevalent flocks is the consequence of the dynamics of the infection of the flocks (Katsma et al. 2005).

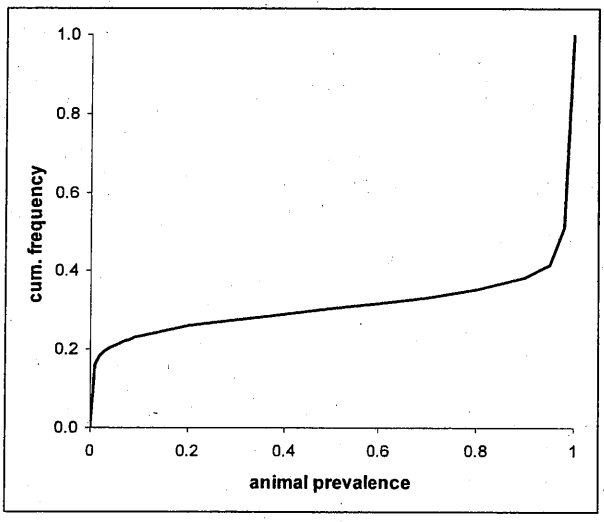

Figure 3.6. Animal prevalence reflects the percentage of birds colonized with Campylobacter in an infected flock, that is with a value of $C_{fec} > 0$.
It is assumed that all birds in a flock are always contaminated at their exterior, due to the frequent contacts between birds and their droppings at the farm and during transport.

3.3.2 Concentration in the faeces

An overview of the data collected is given in table 3.11.
Stern et al. (1995) present the mean log cfu campylobacter/gram caecal contents post transport per farm of nine positive broiler chicken farms in the USA. The mean of these means is
6.8 log cfu/g. Mead et al. (1995) found a mean value of 6.4 log cfu/g for animals at 11 positive farms, in a total sample of 155 animals. Fazil et al. (1999) used data of Stern et al. (1995 and unpublished) and from that, including data below the lower count limit, they derive a Normal distribution with a lower mean 4.95 log cfu/g and standard deviation 1.38.
Additionally we obtained unpublished data from Denmark and the Netherlands.
H. Rosenquist et al (unpubl) analysed the caecal contents of five flocks that were tested positive in samples collected one week prior to slaughter in Denmark. We fitted their raw data using Maximum Likelihood Estimation (MLE) methodology. The mean from their data was 6.2 log cfu/g. Surprisingly, they found one flock with 27% positive count values

(>3 log cfu/g), yielding a mean of only 1.46 log cfu/g.

Table 3.11. Overview of literature data on concentrations of Campylobacter in the intestines or the faeces of broiler chicken in log cfu per gram.
The data of Enthoven are used as input of the risk model.

		mean	sd	
Stern et al (1995)	9 farms	6.83	0.58	sd between means of farms
Mead et al (1995)	11 of 15 farms	6.4	0.7	sd between means of farms
	155 animals		1.2	mean sd within-flock
Fazil et al (1999)	Stern data	4.95	1.38	within-flock sd
Enthoven (unpubl)	190 samples	5.35	2.35	all samples
	176 samples	5.58	1.82	positive samples
	38 flocks	5.54	1.64	distr. of means per flock
	29 flocks	6.00	1.52	distr. of means of flocks with 5 pos. samples
			0.73	mean sd within-flock
Rosenquist et al (unpubl)	5 flocks (n=30)	6.22	2.72	sd between means per flock
			1.39	mean sd within-flock
Jacobs-Reitsma et al. (in prep).	5 flocks (n=10)	7.94	0.87	sd between means per flock

Jacobs-Reitsma et al. (in prep.) analysed the caecal contents of five flocks in the Netherlands in 2004. Results are presented in table 3.12

Table 3.12 Count data of caecal contents, collected in 2004 by Jacobs-Reitsma et al. (in prep).
10 birds are sampled per flock. (Flock numbers are indicators).

flock nr.	1	3	4	5	6
mean	9.20	7.77	7.18	7.15	8.38
sd	0.46	0.40	0.74	0.52	0.45

P. Enthoven (unpublished) provided us with a data set sampled in the Netherlands 1991 - 1994. Five faecal samples prior to hanging at the processing plant were taken per flock of 38 flocks and campylobacter concentrations were determined. This data set was very well suited for our purpose, as these are Dutch data from which we can derive both within-flock and between-flock variability. Per flock raw data (i.e. the measured log cfu/g) were fitted to normal distributions, again using MLE methodology. This methodology allows incorporation of data for threshold values: counts smaller than 2 log cfu per gram were below the detection limit, and other counts were too large for the dilutions applied (yielding >5 or >6 log cfu/g values) (Jacobs-Reitsma et al. in prep.). Additional information from enrichment tests performed on the same samples were included in the analysis, as this implies that campylobacter is present, be it at low concentration when counting methods yield no results.

Of the total of 190 samples of 38 positive flocks, 176 were positive for campylobacter (by enrichment). 29 of the 38 flocks were positive for all 5 samples taken per flock. Fig 3.7 shows an overview of the count data of the 176 positive samples.
The results of the analysis of the data of Enthoven are used as input for the baseline model. This is a complete Dutch data set of faecal samples. Data of caecal samples are not used, because the concentration of campylobacter in the caecum is generally considered to be higher than the concentration in faeces leaking from the cloaca during processing.

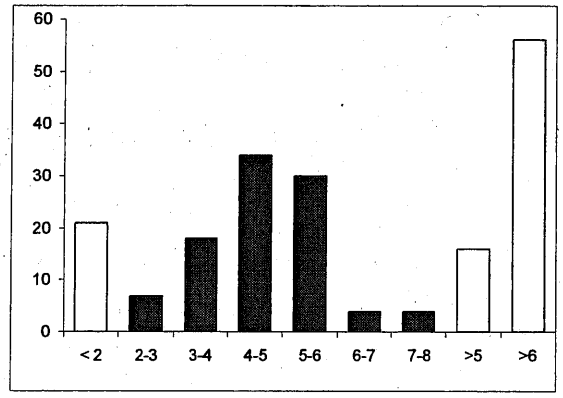

Figure 3.7 The distribution of concentrations of Campylobacter in broiler chicken faeces as found by Enthoven (unpublished results) (n=176).
Bars indicate frequency of classes of concentrations, given in log cfu per gram faeces. Yellow bars are data for which only upper and lower limits are known.

This means we assume a normal distribution of the means per flocks N(6.00, 1.52) log cfu/g. The within-flock variability of infected birds is represented by a standard deviation of 0.73. In the Monte Carlo the upper tail of the distribution is truncated at 10 log cfu/g, to prevent unrealistically high values that may have large impact on the final risk.

3.3.3 Carcass exterior

The contamination of the carcass exterior with campylobacter at the entrance of the processing plant is studied quantitatively by several researchers. Stern et al. (1995) report a (geometric) mean of 7.04 log cfu/carcass. A closer look at their data shows that, when regarding the flocks for which 'normal' transport was simulated only, the mean was 6.4. log cfu per carcass, with a between-flock standard deviation 1.4. Between birds variability cannot be retrieved.
Berrang and Dickens (2000) found 4.7 (sd 0.5) log cfu/ml rinsing water, before scalding, in 300 ml per carcass for 25 carcasses. That yields a mean value of 7.2 log cfu per carcass. From the published 95% confidence interval of the mean the standard deviation between flocks can be assessed at 1.25. Rosenquist et al. (2003) used neck skin data published by Mead et al. (1995). It is not straightforward how to relate these data to numbers per carcass.
For the CARMA project four flocks were sampled at the entrance of a Dutch processing plant, which were previously tested positively at the farm (Jacobs-Reitsma et al. in prep.). Twenty carcasses were taken from the processing line, just after bleeding and just before

entering the scalding-tank. Each carcass was placed into a plastic bag, 100 ml or 1000 ml of Peptone saline was added, and carcasses were washed by hand massage for 30 seconds each. During this washing, special attention was given to the prevention of faecal leakage, by plugging or otherwise. Campylobacter numbers were determined in the rinse water. Normal distributions were fitted through the logs of the counts per flock, using Maximum Likelihood Estimation methods. These distributions thus represent the variability within the flocks. For one small flock, which may be considered not representative for flocks used for chicken meat consumption as it was reared in an experimental setting at a research institute, the best fitting distribution was Normal (5.58, 1.07) in a sample of 15 birds. Results for the other three (representative) flocks are given in table 3.13. The overall mean is 7.27 log cfu/carcass, close to the data of Berrang et al. (2000) and Stern et al. (1995). The mean standard deviation within a flock is 0.56, the standard deviation of the mean is 0.83, but based on a sample of three flocks only.

Table 3.13 Mean and standard deviation of the normal distribution fitting through the log count data of campylobacters on the carcass exteriors of three Dutch flocks in the summer of 2004 (Jacobs-Reitsma et al. in prep.). For each flock, n=20.

flocks	1	2	3
mean	8.03	7.39	6.39
sd	0.50	0.50	0.69

In the CARMA risk model we apply these distributions. Samples are truncated at 4.5 at the lower tail and 10 at the upper tail, as the standard deviation between flocks is based on a sample of 3 only, and to prevent too extreme values.
As stated in the section on animal prevalence we assume that all birds are contaminated at their exterior when they enter the processing plant, irrespective of intestinal colonization. Samples of the distribution of N_{ext} are adjusted for animal prevalence < 100%, as smaller amounts of Campylobacter from chicken faeces will be spread through the flock if animal prevalence is lower. The (within-flock) mean of the normal distribution for log $N_{ext,input}$, sampled from the between-flock distribution Normal (7.27, 0.83), is lowered by the log of the animal prevalence, log (P_{anim}), to obtain the mean applied as within-flock mean.

Table 3.14 Parameter table of the baseline model.
A list with all parameters used in the risk model. Bold parameters are variable and sampled from distributions. Default values are those applied in the baseline model.

stage	parameter	description	unit	default value	reference / source	comment
entrance processing plant	P_{flock}	flock prevalence		44.4 %	Katsma et al. (2005)	
	P_{anim}	animal prevalence in infected flock		see fig 3.6	Katsma et al. (2005)	
	$C_{fec\ \mu}$	concentration in faeces	log cfu/g	6	P. Enthoven (pers. comm.)	max = 10
	$C_{fec\ \sigma}$	sd between birds within a flock		0.73	P. Enthoven (pers. comm.)	
		sd of μ between flocks		1.52	P. Enthoven (pers. comm.)	
	$N_{ext,input\ \mu}$	number campy on exterior	log cfu/ broiler	7.27	Jacobs-Reitsma et al. (in prep.)	max =10, min = 4.5
	$N_{ext\_input\ \sigma}$	sd between birds within a flock		0.56	Jacobs-Reitsma et al. (in prep.)	
		sd of μ between flocks		0.83	Jacobs-Reitsma et al. (in prep.)	
(low) scalding	a_{ext}	transmission ext -> env		0.86	expert study	median
	$1\text{-}a_{fec}$	transmission int -> ext		1.40E-06	expert study	median
	b_{env}	transmission env -> ext		6.80E-06	expert study	median
	c_{ext}	removal ext		0.71	expert study	median
	c_{env}	removal env		0.036	expert study	median
	p_{fec}	prob. leaking faeces		0.48	expert study	median
	$m_{s\ \mu}$	leaking faeces (given leakage)	g	1.84	expert study	median
	$m_{s\ \sigma}$	sd (lognormal)		0.001	guess	
defeathering	a_{ext}	transmission ext -> env		0.91	expert study	median
	$1\text{-}a_{fec}$	transmission int -> ext		1.03E-05	expert study	median
	b_{env}	transmission env -> ext		9.85E-04	expert study	median
	c_{ext}	removal ext		0.049	expert study	median
	c_{env}	removal env		0.11	expert study	median
	p_{fec}	prob. leaking faeces		0.70	expert study	median
	$m_{s\ \mu}$	leaking faeces (given leakage)	g	1.72	expert study	median

	$m_{s\,\sigma}$	sd (lognormal)		0.001	guess	
evisceration	a_{ext}	transmission ext -> env		0.46	expert study	median
	1-a_{fec}	transmission int -> ext		2.75E-03	expert study	median
	b_{env}	transmission env -> ext		1.07E-05	expert study	median
	c_{ext}	removal ext		0.042	expert study	median
	c_{env}	removal env		0.085	expert study	median
	p_{fec}	prob. leaking faeces		0.68	expert study	median
	$m_{s\,\mu}$	leaking faeces (given leakage)	g	1.94	expert study	median
	$m_{s\,\sigma}$	sd (lognormal)		0.001	guess	
washing	a_{ext}	transmission ext -> env		0.31	expert study	median
	b_{env}	transmission env -> ext		2.75E-03	expert study	median
	c_{ext}	removal ext		0.245	expert study	median
	c_{env}	removal env		0.062	expert study	median
(air) chilling	a_{ext}	transmission ext -> env		0.061	expert study	median
	b_{env}	transmission env -> ext		3.75E-03	expert study	median
	c_{ext}	removal ext		0.035	expert study	median
	c_{env}	removal env		0.015	expert study	median
cutting	α	parameter beta distribution partitioning		1	guess	
	frac μ	mean rel. proportion of campy on breast cap		24%	J.Obdam (pers. comm.)	
	z	relative contribution of carcass i to contamination of fillet i		0.17	J.Obdam (pers. comm.)	guess
	log π	fraction of carcass contamination on fillet		-1.8	J.Obdam (pers. comm.)	based on other bacteria
(cool) storage	$r_{storage}$	reduction by storage	log red.	BetaPert (0.1,0.9,2.1)	Jacobs-Reitsma et al. (in prep.)	
consumer prep.	$t_{C,H}$	transfer chicken to hand		0.0415	Montville et al. (2001)	refitted raw data.
	$t_{C,B}$	chicken to board		0.0125	Kusumaningrum et al. (2004)	
	$t_{H,S}$	hand to salad		0.207	Montville et al. (2001)	id

	$t_{B,S}$	board to salad	0.343	Kusumaningrum et al. (2004)	
	$t_{H,H}$	hand wash effect	0.0347	Chen et al. (2001)	id
	$t_{B,B}$	board wash effect	0.0000464	Cogan et al. (2002)	
	$t_{S,S}$	salad wash effect	0.367	Smith et al. (2003)	
	f_{cf}	frequency chicken cut before salad on same board	50%	guess	
	f_{hw}	hand washing frequency	80%	Doorduyn et al. (in prep a)	rough average
	f_{nsb}	frequency not using same boardside unwashed	95%	Doorduyn et al. (in prep a)	rough average
	f_{bw}	frequency board washing	65%	Doorduyn et al. (in prep a)	rough average
	f_{sw}	salad washing frequency	60%	Worsfold and Griffith (1997)	rough average
		various consumption data	see table 3.8 and 3.9	Kistemaker et al. (1998)	
Dose-response	α	Beta distr. dose-infection	0.145	Teunis and Havelaar (2000)	classic model
	β	Beta distr. dose-infection	7.59	Teunis and Havelaar (2000)	classic model
	$P_{ill \mid inf}$	prob. of illness given infection for adults	33%	Havelaar et al. (2000)	classic model and new model adults
	α	Beta distr. dose-infection	0.024	Teunis et al. (2005)	new model
	β	Beta distr. dose-infection	0.011	Teunis et al. (2005)	new model
	ν_y	hazard function illness (young)	3.63E-09	Teunis et al. (2005)	new model
	r_y	hazard function illness (young)	244,000,000	Teunis et al. (2005)	new model
	young meals	number of chicken fillet with salad meals 14-	9,000,000	CBS	
	adult meals	number of chicken fillet with salad meals 15+	76,000,000	CBS	

3.4 Interventions

3.4.1 Selection of interventions

One of the main interests of risk management in the CARMA project is the evaluation of the effects of potential interventions in the poultry meat chain. Here we study these effects in terms of decrease in the assessed number of cases. The relative risk of an intervention is the assessed number of cases after intervention divided by the assessed number in the baseline scenario. The risk reduction is one minus the relative risk.
The evaluated interventions are selected in close collaboration with the risk managers in the CARMA steering committee (with representatives of the ministries of Public Health and Agriculture, Nature and Food Quality). There are some interventions at the farm stage, some at the processing stage and some at the consumer stage, which allows comparison of interventions at different stages. Some interventions are considered on the basis of international experience (like freezing of poultry meat, (Stern et al. 2003)), others because experts expect they will have considerable effect. In the model, we can also evaluate interventions which are currently illegal (like decontamination of processed meat) or the topic of public debate (like irradiation). By evaluation we can add information to the public debate about these issues, without making any statement about social acceptability. The latter is analyzed elsewhere in the CARMA project (Bogaardt 2005).
The selected interventions are summarized below and listed in table 3.15. For a more detailed description of these interventions see Mangen et al. (2005b) and Katsma et al. (2005).

I Thinning
During rearing at the farm, in about 44% of the flocks a small part of the flock is taken away for slaughter and processing about a week before the rest of the flock (thinning). As a consequence catchers have to enter the farm house, which may introduce Campylobacter into the flock. As an intervention, thinning could be forbidden to prevent this potential introduction of Campylobacter.

II Mono-species farms
According to Bouwknegt et al. (2004) 190 of 457 (42%) farms keep at least one other farm animal species. The odds ratio of Campylobacter contamination at these farms was 1.88 times larger than on farms with only broilers. Hence, it was suggested that restricting the presence of other farm animals (or requiring the absence of other farm animals) may be a potentially effective intervention

III Improved hygiene at the farm
Campylobacter enters the poultry meat production chain at the farm. Although good hygiene already gets considerable attention at poultry farms, improved hygiene seems an obvious intervention to prevent the introduction of Campylobacter into broiler chicken flocks.

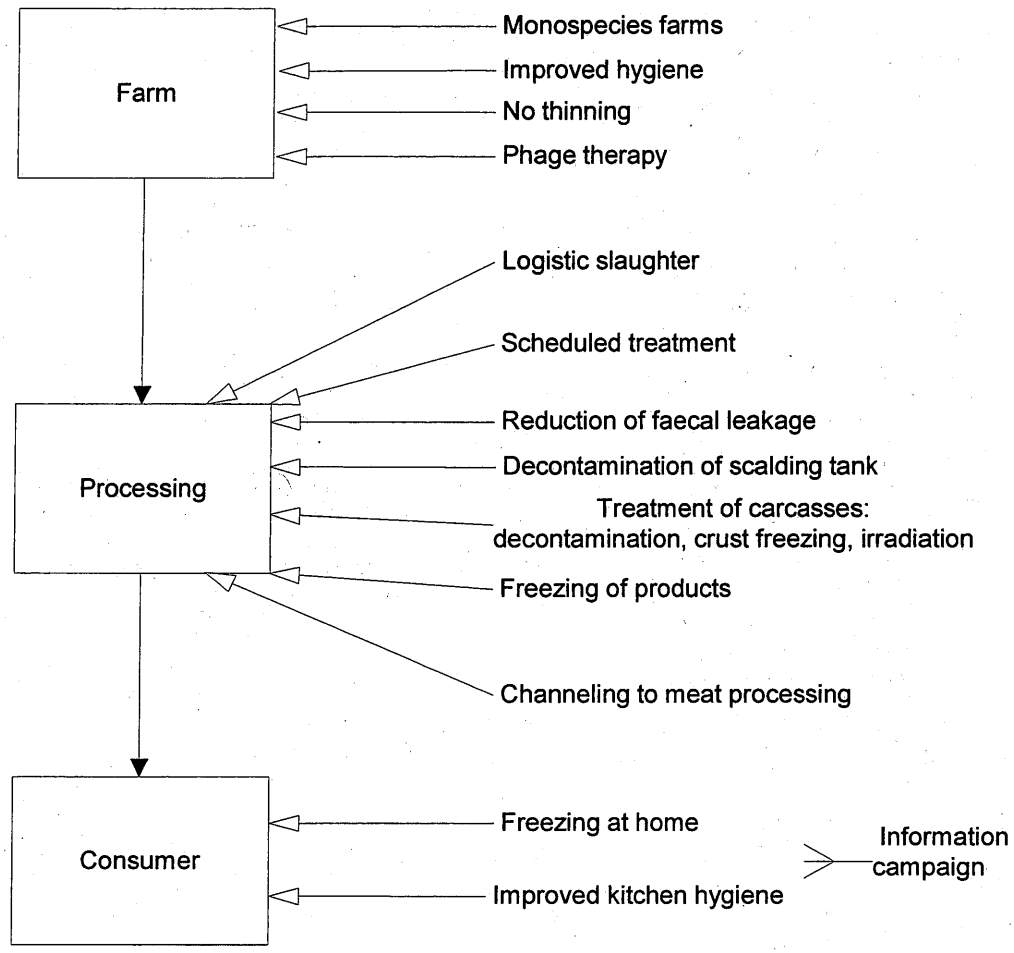

Figure 3.8 An overview of the evaluated interventions in the broiler meat production chain.

IV Phage therapy

Phage therapy, administered at the broiler chickens before slaughter, may reduce the Campylobacter concentration in the gut by 2-3 log units (Wagenaar et al. 2001). As a consequence it may lower the amount of Campylobacter introduced into the poultry meat production chain.

V Logistic slaughter

By rescheduling the processing of the flocks processed at the plant on a day, cross-contamination between flocks tested positively and flocks tested negatively for Campylobacter can be prevented. Minimizing cross-contamination between flocks may prevent an increase in the prevalence of birds contaminated with Campylobacter.

VI Reduction of faecal leakage

During the first stages of chicken processing faeces containing Campylobacter may leak from the intestines and contaminate the carcass exterior. Industry could try to reduce this faecal leakage. Additional processing equipment may for example press faeces close to the cloaca

out of the carcass and wash it away before the carcasses enter the scalding tank. Like phage therapy this will lower the amount of Campylobacter brought into the processing system, and thus lower the levels finally found on the meat. Optimizing the fasting of the birds before slaughter can possibly be considered as another method to achieve the same goal.

VII Decontamination in the scalding tank.
In the scalding tank dirt from carcasses containing Campylobacter may accumulate. Adding a chemical (lactate or TSP (trisodium phosphate) to the scalding water may inactivate Campylobacter and thus lower the amount of Campylobacter brought forward into the processing system.

VIII Decontamination of the carcasses
Decontamination with chemicals like lactate and TSP can also be applied at later stages in the processing plant. Adding it to the washing water, spraying it directly on the carcasses between processing stages or adding an extra scalding tank will lower the level of Campylobacter on the carcasses

IX Carcass surface heat treatment
By applying an extra heat treatment after evisceration such as steam pasteurization (12-24 seconds), hot water (80°C for 20 seconds) or dry heat (15 minutes), levels of Campylobacter on the chicken skin may be reduced (Whyte et al. 2003, Corry et al. 2003).

X Crust freezing
Cold air (at about -30°C) can be blown over the carcasses during chilling. This will freeze the chicken surface and inactivate Campylobacter on the skin (Corry et al. 2003).

XI Irradiation
Chicken meat products can be irradiated to kill off all Campylobacter and Salmonella.

XII Freezing of chicken meat
Freezing chicken meat will inactivate Campylobacter. If chicken meat is frozen (e.g. for two weeks at -30 °C), the levels on this meat will be lowered.

XIII Prepared meat
A similar intervention as the previous one is to inactivate Campylobacter by heat treatment of the chicken meat, producing 'precooked' or 'prepared' chicken meat.

XIV Kitchen hygiene.
If the consumer cooks the meat well and acts hygienically in the domestic kitchen by washing hands and equipment and preventing cross-contamination between raw chicken meat and other foods, Campylobacter originating from chicken meat will not be ingested. To achieve this, consumer hygiene education should be improved, for example by launching an information campaign in the mass media.

XV Home freezing of chicken meat by the consumer
Voluntarily freezing the meat in the home freezer by the consumer may be another method to reduce the level of Campylobacter on the broiler chicken meat. This can also be achieved by an information campaign.

An intervention that may be applied in combination with some of those listed above is scheduled treatment. Here, flocks are tested for Campylobacter some days before slaughter. Negative flocks are treated without any further intervention and can be sold as fresh meat. Positive flocks will be treated differently, by additionally applying one of the interventions mentioned. The interventions considered for evaluation in combination with scheduled treatment are indicated in table 3.15.

Table 3.15 List of interventions to control Campylobacter as initially proposed for evaluation.

nr.	intervention	with scheduled treatment?	stage
I	no thinning		farm
II	mono species farms		farm
III	improved farm hygiene		farm
IV	phage therapy	yes	farm
V	logistic slaughter	yes, by definition	processing plant
VI	reduction of faecal leakage		processing plant
VII	decontamination in the scalding tank		processing plant
VIII	decontamination of carcasses	yes	processing plant
IX	carcass surface heat treatment	yes	processing plant
X	crust freezing	yes	processing plant
XI	irradiation	yes	processing plant
XII	freezing of chicken meat	yes	after processing
XIII	prepared meat	yes	after processing
XIV	kitchen hygiene		consumer
XV	home freezing of chicken meat		consumer

3.4.2 Evaluated interventions

The interventions evaluated with the risk model are not identical to those selected as discussed in section 3.4.1. During the project some interventions were not evaluated further for the reasons given below:

II. Mono species farms
In practice it will be very difficult to prevent or forbid the presence of other farm animals on a chicken farm. Farms with other farm animals are usually the smaller farms, which are expected to have a lower flock prevalence of Campylobacter than larger farms (Katsma et al.

2005). Hence the positive effect of eliminating other animals may be counterbalanced by an increase in the number of broiler flocks. See Mangen et al. (2005b) for a detailed discussion.

V. Logistic slaughter
In other publications of the CARMA project we have studied this intervention and found it is not expected to have much impact on the human health burden of Campylobacter (Evers 2004, Havelaar et al. 2004) Negative flocks cross-contaminated by preceding positive flocks will always show a lower proportion of positive carcasses and much lower levels of campylobacter on the carcass surfaces.

IX Carcass surface heat treatment
According to some Dutch experts consulted for the CARMA project, the quality of the meat is too much affected by this intervention, so the end product cannot be sold. (See also James (2004), Mangen et al. (2005b), Havelaar et al. (2005).)

XIII Prepared meat without channeling
This intervention implies that no fresh or frozen meat will be on the market anymore. This not a realistic option.
For intervention VIII, carcass decontamination, it was decided to evaluate both (a) decontamination at three stages: with an extra warm water tank after defeathering, during washing and by spraying during chilling (Snijders et al. 2004) and (b) by submersion between washing and chilling only (Stekelenburg and Logtenberg 2004). The effect of two chemicals will be evaluated for interventions VII and VIII: lactate and TSP (trisodium phosphate). These are found to be among the most suitable chemicals for this purpose (Stekelenburg and Logtenberg 2004).
Scheduled treatment will be evaluated with three different tests (see Katsma et al. (2005) for details): (1) the 'classical' test by culture method, (2) a test using PCR and (3) a test using a novel method with a dipstick.
The evaluated interventions are listed in table 3.16

3.4.3 Effects of interventions

The effects of the interventions in terms of risk reduction are evaluated by translating the effects of individual interventions into modified model parameter values. As the model is partially a mechanistic model, the effects would ideally be defined in terms of these mechanistics. However, data on the effects of the individual interventions on the mechanistics are limited. Data on changes in levels of campylobacter due to chemicals or temperature stress are usually only given in terms of changes in model outputs such as the levels on the chicken skin or chicken meat. Therefore, the effects of most interventions are expressed in terms of effects on the number of Campylobacter on the exterior of the carcass or the meat, N_{ext}.

For each intervention we define a best estimate as the most likely value. Next, to explore the uncertainty of the estimated effects, we define pessimistic and optimistic values for the effect, yielding a lower resp. higher risk reduction.

Table 3.16 List of interventions evaluated with the risk model.

nr.	intervention	with scheduled treatment?	stage
I	no thinning		farm
III	improved farm hygiene		farm
IV	phage therapy	yes	farm
VI	reduction of faecal leakage		processing plant
VII	decontamination in the scalding tank		processing plant
VIIIa	carcass decontamination at three stages	yes	processing plant
VIIIb	carcass decontamination before chilling	yes	processing plant
X	crust freezing	yes	processing plant
XI	irradiation	yes	processing plant
XII	freezing of chicken meat	yes	after processing
XIII	prepared meat	only	after processing
XIV	kitchen hygiene		consumer
XV	home freezing		consumer

In the search for data to estimate the effects of interventions preference is given to data on interventions on whole carcasses (or parts of it further down the processing line) under more or less realistic conditions (= practice) over data not complying to this (= lab).
The following protocol is applied:

- A point estimate is determined per experiment;
- When data from more than one author are available, then the lowest and highest value found are taken as pessimistic and optimistic value (obvious outliers excluded);
- When data from more than one experiment from one author are available, then the range found by this author is increased on both sides by 0.5 log to obtain the pessimistic and optimistic value;
- When only data from one experiment are available, then the range is the value found plus and minus 1 log;
- When (almost) no data are available, then the range is the proposed best value plus and minus 2 log.

I No thinning

The effect of a ban on thinning could not be evaluated directly with the farm model (Katsma et al. (2005); see also Mangen et al. (2005b)). As thinning is not explicitly incorporated in this model, it could not be banned either. As a solution, the opposite was evaluated. The farm model was run assuming that one colonized broiler enters the farm house five days before

slaughter. The resulting flock prevalence is 88%. This finding and the distribution of within-flock animal prevalences was used as input of the processing model to evaluate the effect of thinning in all farms on the relative risk. The effect of a ban on thinning will be comparable with the opposite of this result, that is a decrease of the relative risk comparable to the increase in relative risk as found in the analysis.

III Improved farm hygiene

This scenario is evaluated with the farm model of Katsma et al. (2005). Results in terms of a change in the distribution of within-flock animal prevalences and flock prevalence are evaluated by the processing model.

IV Phage therapy

With this intervention broiler chickens are treated with phages to reduce the level of Campylobacter in the intestines. Wagenaar et al. (2001) have shown that administering phages has an effect of about 2 logs reduction. As this is the result of just one study, it should be considered as rather uncertain.

Lowering the concentration of campylobacter in the faeces may also have an effect on the number of campylobacter on the exterior of the birds. This effect, however, has never been measured.

As an effect of phage therapy in the risk model we take:

Pessimistic: reduction of log $C_{\text{fec}\,\mu}$ by 1 log

Best: reduction of log $C_{\text{fec}\,\mu}$ by 2 log

Optimistic: reduction of log $C_{\text{fec}\,\mu}$ by 2 log and of the mean log $N_{\text{ext, input}\,\mu}$ by 1 log.

VI Reduction of faecal leakage

Here we assume that equipment for reduction of faecal leakage is placed just before the scalding tank. The equipment may for example press the faeces out of the carcass and wash off the dirt, thereby decreasing the faecal leakage during processing. Other equipment with a similar effect can be considered too.

The effect of this intervention is brought in to the model mechanistically. The equipment lowers the amount of leaking faeces and thus lowers N_{fec}, the product of the concentration of Campylobacter, C_{fec}, and the mass of leaking faeces, w_{fec}, at all stages of the processing chain. Although the effect is actually aimed at w_{fec}, the intervention is implemented as a reduction in log C_{fec}, which appeared to be the simplest way to implement the desired effect on N_{fec} in the risk model. Preliminary calculations have shown that a reduction in leakage of campylobacters with faeces with a factor 10 and 10^6 gives a reduction of log N_{ext} of resp. 0.5 and 0.9 (unpublished). The latter reduction resembles a value found by pilot industrial trials with a prototype of equipment as meant for this intervention (data not shown). However, the variability in the effects measured is large.

Therefore we taken:

Pessimistic: $C_{\text{fec}\mu}$ is unaltered

Best: reduction of the mean value of $C_{\text{fec}\mu}$ by 6 logs

Optimistic: $C_{\text{fec}\mu}$ gets zero

VII/VIII Decontamination with lactate

See table 3.17. Data on the reduction of *C. jejuni* on broiler carcasses through lactate are scarce. Van Netten et al. (1994a) and Van Netten et al. (1994b) present good data, describing the effect of pH, temperature and exposure time, however these data are on pork skin suspensions and pork bellies.

Table 3.17 Data collected on the decontamination effects of lactate on chicken carcasses.
P = practice, L = lab

Processing details	species	effect		Reference
Immersion in warm water (< 50 °C) with 0.3 % lactic acid	*C. spp*	0.8-1.2 log	P	Van de Nieuwelaar, (pers. comm.)
Immersion in 0.25 and 0.5 % lactic acid at 50 °C for 90 s	*C. jejuni*	0.25 %: 0.80 0.5 %: 0.77	P	Stern et al. (1985)
Spraying with 2 % lactic acid, 24 h at 4 °C	*C. jejuni*	Naturally contaminated: ≥ 1.6 log; artificially: 1.0 log	P/L	Cudjoe and Kapperud (1991)
Spraying with 1 % lactic acid, 24 h at 4 °C	*C. jejuni*	Naturally contaminated: ≥ 1.2 log; artificially: 0.25 log	P/L	Cudjoe and Kapperud (1991)
Moisten the product with lactic acid during chilling	*C. spp*	0.8 - 1 log	P	Van de Nieuwelaar, (pers. comm.)
2 % lactic acid solution, in pork skin suspension or on pork belly, 30 s at 21 °C	*C. jejuni*	2.5-2.6 log	L	Van Netten et al. (1994a)
1% or 2% Lactic acid solution in pork skin suspension, variation in exposure time, temperature and pH	*C. jejuni*	0.3->5.3*	L	Van Netten et al. (1994b)
10% lactic acid	*C. jejuni*	1 log	?	VVDO (1998)

*The immediate death for *C. jejuni* decreased from 2.6 log to >5.3 log at pH 2.6 to 0.3-1.0 log at pH 4.0. The decrease in bactericidal effect with increasing pH could be countered by an increase in the temperature. Estimated effect in realistic situation: such treatment would suffice to kill up to about 3 log10 cfu in the lactic acid film and up to 0.3 log 10 cfu protected by meat buffering at pH 4.0.

VIII. Decontamination of the scalding tank with lactate

As best estimate, we use the data from Stern et al. (1985). The concentrations used were much lower than 2.5 %, but in their experiment an increase from 0.25 to 0.5 % had no effect on the inactivation of *C. jejuni*, so concentration seems to play a minor role here at 50°C and

an effect of 0.8 log seems reasonable. For the minimum we choose the value of 0.3 log mentioned by Van Netten et al. (1994b) and for the maximum we use the value of 1.2 as mentioned by Van de Nieuwelaar (pers. comm.). So:

Pessimistic: reduction of N_{ext} by 0.3 log
Best: reduction of N_{ext} by 0.8 log
Optimistic: reduction of N_{ext} by 1.2 log

VIIILb Submersion in lactate between washing and chilling

We use the data from Cudjoe and Kapperud (1991) which includes the range given by Van de Nieuwelaar (pers. comm.) for chilling. For the minimum we rounded 0.25 to 0.3, the best estimate is an intermediate value at 2% lactic acid and the maximum of 2 was chosen given the $\geq$ 1.6 log reduction found by them. The estimates of VIIL and VIIILb are thus similar, which is not unreasonable as on the one hand temperature is lower in VIIILb but on the other hand exposure time is longer.

Pessimistic: reduction of N_{ext} by 0.3 log
Best: reduction of N_{ext} by 1.3 log
Optimistic: reduction of N_{ext} by 2 log

VIIIL Decontamination of carcasses with lactate

With this intervention inactivation by lactate is implemented by an extra warm water tank after defeathering, during washing and during chilling. Effectively, compared to VIIILb, the intervention is extended with exposure time to lactate at room temperature. We very roughly estimate that this will increase inactivation by 0.5 log.

Pessimistic: reduction of N_{ext} by 0.8 log
Best: reduction of N_{ext} by 1.8 log
Optimistic: reduction of N_{ext} by 2.5 log

VII/VIII Decontamination with TSP

See table 3.18. We exclude the experiments with lab-type or unknown setup (Anonymous 2003, Keener et al. 2004). The results from Slavik et al. (1994), where the TSP remains on the carcasses after 15 s, indicate that at low temperatures, i.e. storage at 4 °C or 15 s dip at 10 °C, TSP has little effect. This implies that results from Slavik et al. (1994) and Federighi et al. (1996) can be compared and that the effect at 16-20°C and 50°C is similar. It also implies that all data available are effectively on 15 s exposure (plus some cooling down time). We have no data on the relationship between TSP exposure time and inactivating effect.

VIIT Decontamination of the scalding tank with TSP

We exclude the experiment done at 10°C (part of Slavik et al. (1994)). So the best estimate is equal to the mean of (1.5, 1.2, 1.3, 1.03, 1.16) = 1.24. The range is 1.03 1.5. So:

Pessimistic: reduction of N_{ext} by 1.03 log
Best: reduction of N_{ext} by 1.24 log
Optimistic: reduction of N_{ext} by 1.5 log

VIIITb Submersion in TSP between washing and chilling

As stated above, we assume that the temperature effect in the range of 16 50°C is small. As there is no large difference in exposure time (limited in VIIT by further processing, especially washing and in VIIITb by cooling to 10°C), the values are the same as for VIIT:

Pessimistic: reduction of N_{ext} by 1.03 log

Best: reduction of N_{ext} by 1.24 log

Optimistic: reduction of N_{ext} by 1.5 log

Table 3.18 Data collected on the decontamination effects of TSP on chicken carcasses.

Processing details	species	Effect	Practice or lab	Reference
15 s dip into 10 % Trisodium phosphate, storage at 4°C (no showering)	*C. jejuni*	50 °C, 1 day storage: 1.5 log reduction; 50 °C, 6 day storage: 1.2 log reduction; 10 °C, 1 day storage: 0.16 log reduction	Practice, post-chill carcasses	Slavik et al. (1994)
15 s dip into 10 % TSP at 16-20 °C, showering and store at 4°C	*C. spp*	1.3 log reduction	Practice, Naturally contaminated carcasses from local processing plant, whole carcass rinse	Federighi et al. (1996)
15 s 12% TSP-solution	*C. spp*	1.03 log reduction	Practice; whole carcass rinse samples from large broiler processing plants	Bashor et al. (2004)
15 s dip in 10 % TSPat 20°C, storage at 4°C	*C. spp*	Dip in potable water gives 0.55 log reduction; dip in water with TSP gives 1.71 log reduction, so reduction due to TSP is 1.16 log	Practice; TSP treatment on whole carcasses, analysis of neck skins	Whyte et al. (2001)
TSP	*C. jejuni/coli*	5 log	Lab (Artificial biofilms or suspension of cells)	Keener et al. (2004)
Trisodium phosphate	*C spp*	4 log, reduction prevalence from ca. 100 to 30 %	?	Anonymous (2003)

VIIIT Decontamination of carcasses with TSP

In this intervention inactivation by TSP is implemented by an extra warm water tank after defeathering, during washing and during chilling. This gives a longer exposure time than for VIIT and VIIITb, which we roughly estimate as an increase effect of 0.5 log. So:

Pessimistic: reduction of N_{ext} by 1.53 log
Best: reduction of N_{ext} by 1.74 log
Optimistic: reduction of N_{ext} by 2.0 log

X Crust freezing

See table 3.19. As best estimate the mean of (1) and (2) is taken, not including the experiments on freezing of pieces of skin and also not including the value of 0.4 from Mead, which is rather different although based on personal communication by Corry. The mean is (0.9 + 1.2) / 2 = 2.1 / 2 = 1.1. The range is 0.9 to 1.2. As all data are from the same author, 0.5 log is added to the uncertainty on both sides, so a pessimistic and optimistic value of 0.4 and 1.7:

Pessimistic: reduction of N_{ext} by 0.4 log
Best: reduction of N_{ext} by 1.1 log
Optimistic: reduction of N_{ext} by 1.7 log

Table 3.19 Overview of data on the effects of crust freezing

Nr	Method	species	Effect	Practice or lab	Reference
1	Rapid surface freezing ('crust freezing')	*C. jejuni*	0.9 log	Practice (carcasses). From chicken processing plant, inoculated	Corry et al. (2003)
2	Crust freezing	*C. jejuni*	about 1.2 log	Practice (Whole naturally contaminated carcass rinse)	Corry (pers. comm.)
3	Rapid freezing	*C. jejuni*	1-1.5 log	Lab (piece of skin). From chicken processing plant, inoculated	Corry et al. (2003)
4	Crust freezing	*C. jejuni*	about 1 log	Lab (Breast skin). From inoculated carcasses	Corry (pers. comm.)
5	Crust freezing	*C. spp*	0.4	carcasses	Mead (2004)

XI Decontamination by irradiation.

Food irradiation can be done with ionizing radiation and this can be electron radiation, X-rays or gamma rays. The SI unit of absorbed dose is the gray (Gy). It is defined as the mean energy imparted by ionizing radiation to matter per unit mass. One Gy is equal to one joule per kilogram (WHO/FAO 1988). Penetrating depth of Gamma and X-ray is 80-100 cm, of E-

beam 8-10 cm (Puridec 2004). D_{10} values are radiation doses needed to reduce the number of specific micro-organisms in specific foods by a factor of 10.
As for legal obligations in The Netherlands, in 1983 the Dutch parliament conformed to the WHO vision that 10 kGy can be applied without adverse consequences (Neijssen 1988a). In 1988, the maximum dose for decontamination of poultry by irradiation was 3 kGy (WHO/FAO, 1988). In 1992, the maximum permitted dose for microbial control of poultry by ionizing radiation was 10.5 kGy (Farkas 1998). At present, the maximum permitted dose for poultry meat in the Netherlands is 7 kGy (Rietveld 2002). In the United States, FDA and USDA have approved irradiation of chicken at a maximum dose of 3 kGy to control foodborne pathogens such as Salmonella and Campylobacter (Keener et al. 2004)
As a strategy for choosing the best D_{10} estimate (table 3.20), considerations were that on the one hand (1) and (3) are based on a number of references and (2) and (4) on only one and that on the other hand (1) and (3) are not specifically on poultry, whereas (2) and (4) are on poultry. Therefore the midrange values of (1)-(4) were given equal weight. Apart from this, the midrange values are not very different, so different strategies will not influence the outcome much. So as the best estimate the mean of the midrange values for chilled meat, 0.17, 0.185, 0.22, 0.175 is taken, which is 0.19 kGy. For the range simply the largest reported range is taken, which is 0.12-0.32 kGy.

Table 3.20 Overview of data on the effects of irradiation.

No.	Method	Species	Effect	Reference
1	Ionising radiation, Summarizing range of D_{10} values (kGy) of many labs in meat and poultry	*C. jejuni*	Non-frozen: 0.14-0.20; frozen: 0.21-0.32.	Farkas J (1996)
2	Ionising radiation in poultry meat, D_{10} values (kGy)	*C. jejuni, C. coli, C. fetus*	0.12 to 0.25 kGy, more sensitive than Salmonella and L. monocytogenes	Keener et al. (2004)
3	Irradiation D_{10}-values	*C. spp*	0.12-0.32 kGy in chilled meat	Corry and Atabay (2001)
4	Ionizing radiation D_{10} values	*C. jejuni in ground turkey*	Non-frozen = 0.16-0.19; frozen = 0.293	Farkas (1998)

As for recommended doses, an FAO/IAEA/WHO Expert committee advised in 1976 a dose of 2-7 kGy for decontamination of chicken. A joint WHO committee stated in 1980 in Geneva that irradiation of any food commodity up to an overall average dose of 10 kGy presents no toxicological hazard and that it introduces no special nutritional or microbiological problems (WHO/FAO 1988). The Dutch Health Council stated in 1988, conforming to WHO, that doses that are effective in eliminating pathogens such as Campylobacter (2-4 kGy) are no threat to public health (Gezondheidsraad 1988). According to Neijssen 1988b organoleptic changes to food products can occur at doses of 1-10 kGy.

These effects are strongly reduced by freezing prior to irradiation. In 1997, WHO stated that food exposed to doses greater than 10 kGy are nutritionally adequate and safe from a toxicological and microbiological point of view (WHO 1997).
We comply to the more careful approach of Farkas (1996, 1998) who gives as recommended doses for organoleptic acceptability of radiation processing 1.5-2.5 kGy for chilled poultry and 3-5 kGy for frozen poultry. Using the D_{10} values derived above, this leads to the following estimates for reduction of *C. jejuni* by irradiation:
Pessimistic: reduction of N_{ext} by 1.5/0.32 = 4.7 log
Best: reduction of N_{ext} by 2.0/0.19 = 10.5 log
Optimistic: reduction of N_{ext} by 2.5/0.12 = 20.8 log

XII Freezing of chicken meat
Sandberg et al. (submitted) investigated half chicken carcasses that were put into the freezer (at -18°C) for different time periods. Quantitative culturing was conducted from a 10 g sample. The log reduction was about 1 after 10 days and 2 after 21 days. Assuming a linear relationship this implies a reduction of log 1.36 after 14 days.
Ritz-Bricaud et al. (2003) investigated the effect of freezing at -20°C with two methods (counting and MPN), on the skin, below the skin and on the muscle, analyzing samples of 5 cm^2 of surface. She found 0.9-3.2 log decline in two weeks (Ritz, unpublished data). Freezing for more than two weeks yielded no additional effect of freezing, in agreement with similar findings of Moorhead and Dykes (2002) and Bhaduri and Cottrell (2004). Hence, two weeks is considered to be the optimum freezing time with regards to the effects on Campylobacter.
As best estimate the mean is taken of 1.36 and ((0.9+3.2)/2)= 2.05; this is 1.7. The range is 0.9 -3.2, which includes the value from Sandberg. As we have data from more than one author, the range is not increased further.
Pessimistic: reduction of N_{ext} by 0.9 log
Best: reduction of N_{ext} by 1.7 log
Optimistic: reduction of N_{ext} by 3.2 log

XIII Prepared meat of chicken from positively tested flocks, with scheduled treatment
It is assumed that this intervention fully inactivates Campylobacter.

XIV Information campaign on kitchen hygiene
Here we aim at performing an information campaign through the mass media aimed at change of behaviour during preparation of raw chicken breast fillet such that cross-contamination in the kitchen is reduced.
In a previous report (Nauta et al. 2001) research was done on the effect of an information campaign. It appeared that the effect on behaviour as a result from an information campaign to the general public is poorly known and depends on several factors, including for example the specificity of the campaign (target group, subject), properties of the target group and how well the campaign is prepared by proper research. It is doubtful whether television is a suitable medium to achieve a change in behaviour. Interventions on a specific target group in

a frequently visited setting (for example a supermarket or a school) and with a more personal approach could make an important contribution additional to an information campaign.
The limited amount of quantitative data that was obtained, points to a maximum of 7 % of the people changing their behaviour in reaction to any kind of information. As intervention XIV is a mass media campaign and given the doubts above, a value of 3 % is taken as a rough best estimate. No effect of a campaign is taken as pessimistic estimate. So:

Pessimistic: 0 % of the people change their behaviour
Best: 3 % of the people change their behaviour
Optimistic: 7 % of the people change their behaviour

These values are implemented by assuming that the frequency of people performing non-hygienic behaviour changes with the percentages mentioned above.
As non-hygienic behaviours we selected 'not washing hands' and 'using the same cutting board for meat and salad'. Thus, the frequency of hand washing f_{hw} and the frequency of not using the same board side f_{nsb} change due to the information campaign. In the evaluation of alternative scenarios it was found that these parameters have the highest impact on risk reduction (see also Mylius et al. (submitted)).

XV Freezing of chicken meat products by the consumer
Here we aim at performing an information campaign through the mass media aimed at stimulating the consumer to put their chicken meat in the freezer for at least a day prior to consumption. The effect of this intervention is the combination of the effect on human behaviour and of freezing.
The effect of an information campaign through the mass media is taken from intervention XIV:

Pessimistic: 0 % of the people change their behaviour
Best: 3 % of the people change their behaviour
Optimistic: 7 % of the people change their behaviour

For the effect of freezing, we make use of the estimates from intervention XII, which are for a freezing time of 14 days. We assume that the mean storage time of the chicken fillet in the freezer in intervention XV is 2 days. This based on the assumption that most Dutch consumers will not buy fresh meat for long term frozen storage, but merely put it in the freezer for a few days by habit. The values for intervention XV are obtained by dividing the estimates from intervention XII by 7. So:

Pessimistic: reduction of N_{ext} by 0.13 log
Best: reduction of N_{ext} by 0.24 log
Optimistic: reduction of N_{ext} by 0.46 log

This intervention is implemented by combining the changes in parameter values for the pessimistic, best and optimistic effects. So pessimistic there is no change, best 0.24 log reduction of N_{ext} for 3% of the meals and optimistic best 0.46 log reduction of N_{ext} for 7% of the meals

Table 3.21 Overview of the effects of the interventions on the model parameters as implemented in the risk model.
Best estimates are given in bold.

nr.	Intervention	target parameter	pess / best / opt effect
I	thinning	Farm Model (Katsma et al. 2005)	
III	improved farm hygiene	Farm Model (Katsma et al. 2005)	
IV	phage therapy	log C_{fec} (log N_{input})	-1 (0)/ **-2 (0)**/ -2 (-1)
VI	reduction of faecal leakage	log C_{fec}	-0 / **-6** / - ∞
VII L	decontamination in the scalding tank	log $N_{ext, scald}$	-0.3 / **-0.8** / -2
VII T	decontamination in the scalding tank	log $N_{ext, scald}$	-1.03 / **-1.24** / -1.5
VIIIL	decontamination at three stages (lactate)	log $N_{ext, def}$; log $N_{ext, wash}$; log $N_{ext, chill}$	-0.27 / **-0.60** / -0.83 -0.27 / **-0.60** / -0.83 -0.27 / **-0.60** / -0.83
VIII Lb	decontamination before chilling (lactate)	log $N_{ext, wash}$	-0.3 / **-1.3** / -2
VIII T	decontamination at three stages (TSP)	log $N_{ext, def}$; log $N_{ext, wash}$; log $N_{ext, chill}$	-0.51 / **-0.58** / -0.67 -0.51 / **-0.58** / -0.67 -0.51 / **-0.58** / -0.67
VIII Tb	decontamination before chilling (TSP)	log $N_{ext, wash}$	-1.03 / **-1.24** / -1.5
X	crust freezing	log $N_{ext, wash}$	-0.4 / **-1.1** / -1.7
XI	Irradiation	log $N_{ext, chill}$	-4.7 / **-10.5** / -20.8
XII	freezing of chicken meat	log $N_{ext, f}$	-0.9 / **-1.7** / -3.2
XIII	prepared meat	$N_{ext, def}$	= **0** (all inactivated)
XIV	kitchen hygiene	f_{hw} ; f_{nsb}	0 /+ **0.01** / + 0.03 0 / + **0.002** / + 0.004
XV	home freezing	log $N_{ext, fs}$; Probability of effect on log $N_{ext, fs}$	-0.13 / **-0.24** / -0.46 0% / **3%** / 7%

3.4.4 Alternative scenarios

A set of alternative scenarios is analysed to explore the sensitivity and uncertainty of the risk model. Parameters at all stages are chosen to compare sensitivity all along the chain.
(1) The sensitivity for the mean values of N_{ext} and C_{fec} is studied, to explore the sensitivity of the model output (relative risk) for both of these rather uncertain input parameters.
(2) As quite some effort has been made to incorporate variability between flocks and birds into the model, the impact of taking variability into account is analyzed.
(3) In the risk model analysis the uncertainty in parameter estimates for the processing model, resulting from the expert study (Van der Fels-Klerx et al. 2005), is omitted. Only the median of the expert estimates are taken into account. Therefore the impact of this uncertainty is

studied separately by excluding between-flock variability and adding uncertainty. Also, uncertainty as a result of choices made during the expert study is studied.
(4) The modelled effects of carcass cutting and storage are very uncertain, based on expert opinion and a few data only. The impact of this uncertainty is analysed.
(5) The estimated parameters values for frequencies of consumer food handling are quite uncertain, based on few data and some assumptions. The impact of this uncertainty is analyzed too.
(6) Finally, the effect of the choosing alternative dose-response models is studied.

4. Results

4.1 Baseline

As a baseline, the risk model is run with the baseline values as given in table 3.14. These values aim to represent the best estimates of the parameter values as currently available. The model represents the situation of broiler chickens processed in the Netherlands in the year 2000. (The year 2000 is chosen at the start of the project, as this was a recent year without any crisis in animal agriculture in the Netherlands.) In the baseline variability between birds in a flock and variability between flocks is included, uncertainty in parameter values is not taken into account.

First, for a better understanding of the dynamics, the processing model is run without incorporation of between-flock variability and with animal prevalence $P_{anim} = 100\%$, and mean and within-flock standard deviation of log ($N_{ext, input}$) and log (C_{fec}) as given in table 3.14. This represents the effect of industrial processing on an average flock with all animals colonised with Campylobacter. The mean result of 3000 runs of this model (with 500 carcasses of this average flock), is illustrated in fig 4.1. To get an impression of the variability between carcasses within flocks, the mean values are taken of the percentiles of the within-flock variability distribution of 500 carcasses, as generated by each of the 3000 model iterations. This variability between carcasses decreases due to the effects of cross-contamination. After chilling, 90% of the carcasses have a value of log ($N_{ext, chill}$) between 4.17 and 5.22. There is a continuous decrease in log (N_{ext}) over the stages, a total mean decrease of 2.65 logs from input to chilling, from 7.27 to 4.62. The variability between the runs is small, and solely the effect of stochasticity (the 90% CI of log ($N_{ext, chill}$) is <4.58, 4.67>). After cutting, the mean value of log ($N_{ext, f}$) is 2.04 (90% CI <1.99, 2.10>).

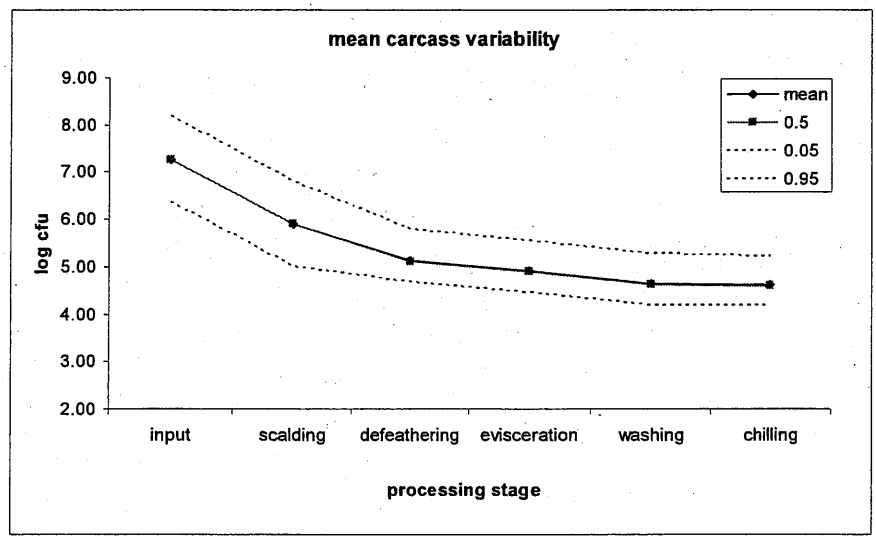

Figure 4.1 The effects of processing on log (N_{ext}) for an average flock with P_{anim} = 100%. The mean values of 3000 iterations of the baseline model are shown without between-flock variability. The variability as represented by the percentiles is the mean within-flock (between carcass) variability.

The results of the baseline model including between-flock variability (and thus representing the population of flocks in the Netherlands) are presented in table 4.1 and illustrated in figs 4.2 - 4.7. One model run consists of 5000 iterations and simulates 5000 independent flocks, with varying animal prevalence and varying mean values of log ($N_{ext, input}$) and log (C_{fec}), as indicated in table 3.14. Due to the presence of flocks with lower animal prevalence, the mean value of log $N_{ext,input}$ (6.71) is lower then 7.27, as explained in section 3.3.3. With inclusion of between-flock variability the mean value of log (N_{ext}) after chilling is 4.36 and the mean effect of processing is a reduction of 2.35 logs. Hence, both the level after processing and the effects of processing are lower as in the case of a single average flock.
Now, due to *between*-flock variability, the variability between carcasses *within* flocks varies itself. To get an impression of the within-flock variability, the mean values are taken of the percentiles of the within-flock variability distribution of 500 carcasses, as generated by each of the 5000 model iterations. (So, for example, the value given in table 4.1 for the 5%-ile is the mean of 5000 5%-iles of the within-flock distribution of 5000 flocks.) Again, this variability between carcasses decreases due to the effects of cross-contamination. (see figs 4.2 and 4.3). After chilling on average 90% of the carcasses have a value of log ($N_{ext, chill}$) between 3.82 and 5.02.
The variability *between* flocks is expressed by taking the variability of the means of each iteration. This variability is large and increases with processing (see fig 4.4 and 4.5). Its distribution is further illustrated by fig 4.6, by comparing the means of 5000 flocks at the input and after chilling and cutting. To compare the effects of the between-flock variability in input values of $P_{anim,}$ log (C_{fec}) and log ($N_{ext, input}$), a sensitivity analysis is performed, correlating the input distributions with the output (log $N_{ext, f}$). The results are shown in fig. 4.7, indicating that for all three input distributions the variability in the input values is correlated with the variability of the output, so all have considerable impact.
For a better understanding of the effects of variability in input between flocks, figs 4.8 and 4.9 show the mean results for the change in log (N_{ext}) if the model is run with slightly modified input. If the animal prevalence does not vary between flocks, but is fixed for different values of the animal prevalence (fig 4.8), the curvature of the effect of processing is similar, but the position changes. With P_{anim} = 1% the mean value of log ($N_{ext, chill}$) = 2.57, with P_{anim} = 10% the mean value of log ($N_{ext, chill}$) = 3.86 and with P_{anim} = 100% the mean value of log ($N_{ext, chill}$) = 5.03. (Note that the latter is larger than the value 4.62 for the 'average flock' shown in fig 4.1, for which variability in N_{ext} and C_{fec} is excluded.) If the mean values of log($N_{ext, input}$) and log (C_{fec}) are lowered by two log units, the curvature of the effect of processing changes (see fig 4.9). With lower log($N_{ext, input}$) the initial level is lower, but log(N_{ext}) increases during defeathering due to faecal leakage. With lower log(C_{fec}) the initial value of log(N_{ext}) is unaltered, but decreases faster, due to a smaller effect of faecal leakage.

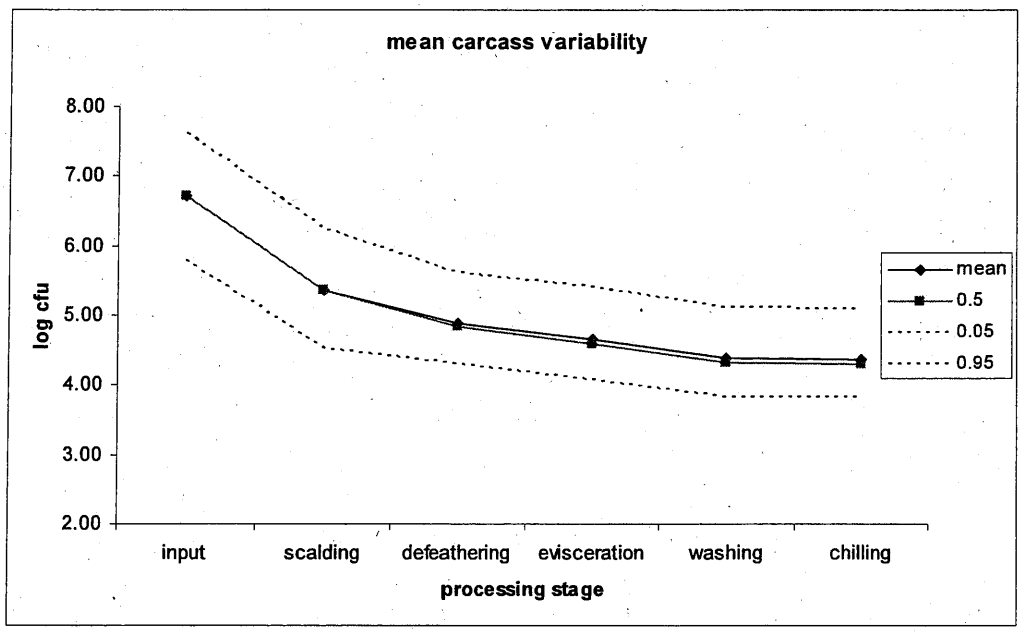

Figure 4.2. The effect of processing on the within-flock variability of log(N_{ext}) over the processing stages.
The graph shows the mean of the within-flock distribution, and the mean 5%, 50% and 95%-iles. N_{ext} decreases and the variability decreases too.

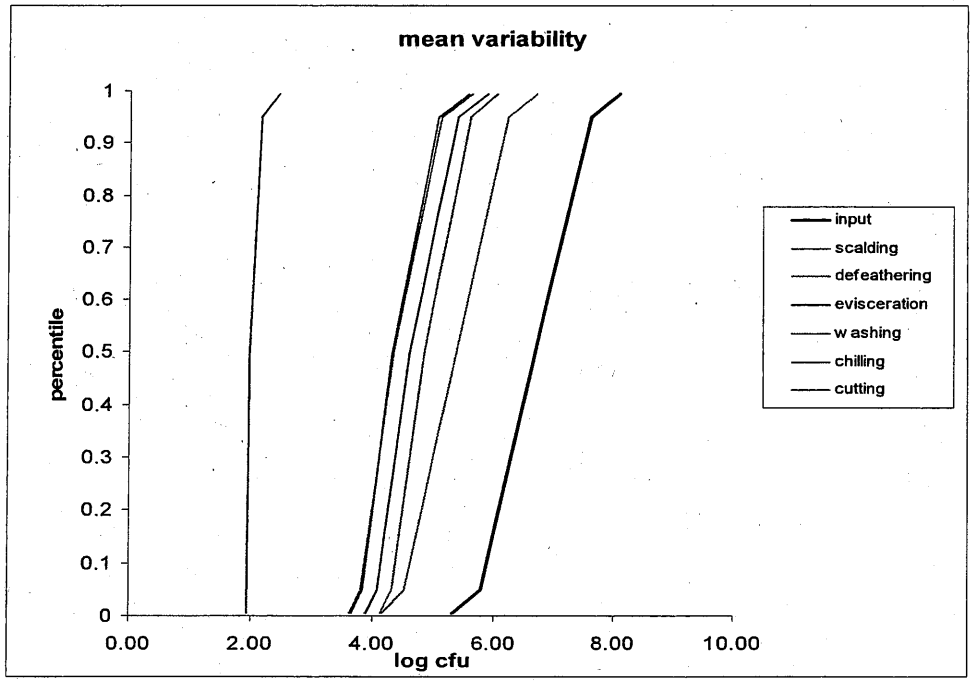

Figure 4.3 The distributions of the mean within-flock variability represented as cumulative distributions for the consecutive stages of processing until cutting.
Scalding and cutting have the largest effect in decreasing the number of cfu per unit. After cutting the variability is much lower, due to cross-contamination during cutting.

Table 4.1 Means and distributions of log (N_{ext}) in the baseline of the processing model.
The columns give the values for the input and the processing stages scalding to chilling. 'Effect' shows the results for the processing effect until chilling. The last column shows the values after cutting (log ($N_{ext,f}$)). As results are expressed in log units, they are for contaminated units only. Mean and sd in the first two rows are the mean of the mean values for 500 carcasses per flock, for all 5000 iterations, and the mean of the standard deviations per iteration. Means of percentiles indicate the mean variability within flocks, and the percentiles of the mean represent the variability of the mean values per flock. The mean effect is positive in 3% of the iterations, indicating that N_{ext} increases due to processing in 3% of the flocks. The mean prevalence of contaminated fillets from a contaminated flock after cutting is 94%.

	input	*scalding*	*defeathering*	*evisceration*	*washing*	*chilling*	*effect*	*cutting*
mean	6.71	5.37	4.88	4.65	4.38	4.36	-2.35	1.97
sd	0.56	0.53	0.40	0.41	0.41	0.39	0.38	0.09
Means of the percentiles (mean variability within flocks)								
0.005	5.31	4.14	4.12	3.88	3.63	3.64	-2.92	1.94
0.05	5.80	4.53	4.31	4.07	3.82	3.82	-2.81	1.94
0.5	6.71	5.36	4.83	4.60	4.33	4.31	-2.43	1.97
0.95	7.63	6.25	5.60	5.40	5.12	5.08	-1.62	2.15
0.995	8.12	6.73	6.05	5.91	5.63	5.58	-1.03	2.44
Percentiles of the mean (variability between flocks)								
0.05	4.36	3.00	2.18	1.90	1.63	1.63	-2.90	0.00
0.5	6.90	5.56	5.07	4.84	4.57	4.54	-2.74	2.02
0.95	8.43	7.05	6.88	6.72	6.45	6.43	-0.49	3.87

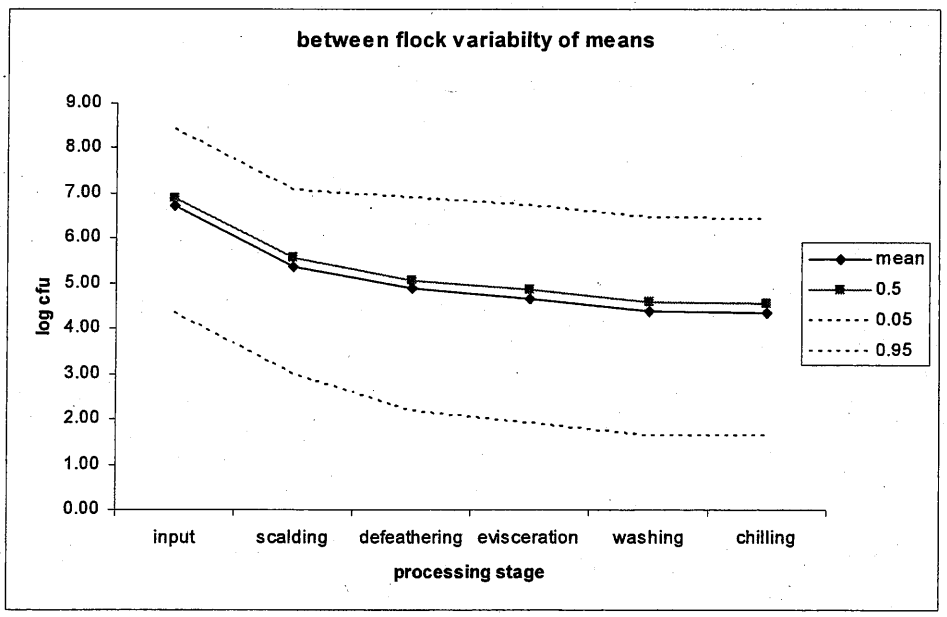

Figure 4.4 The effect of processing on the between-flock variability of the means of log(N_{ext}) per flock.
The graph shows the mean of the between-flock distribution, and the 5%, 50% and 95%-iles. N_{ext} decreases and the variability slightly increases.

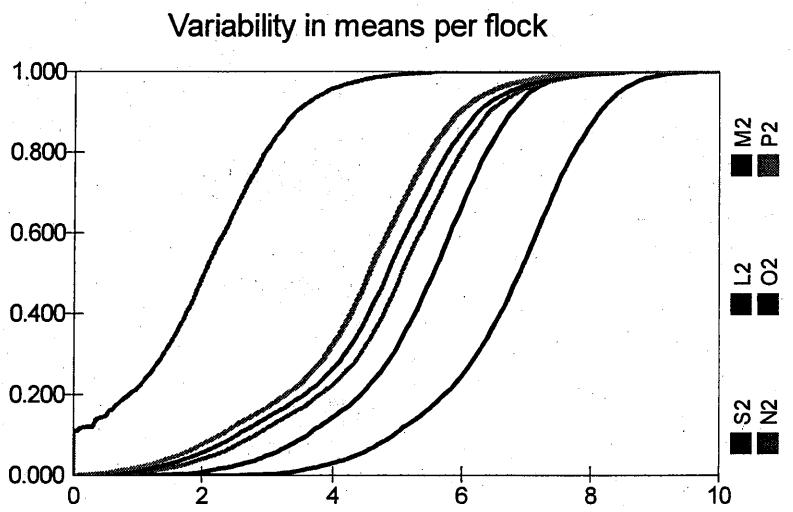

Figure 4.5 The distributions of the between-flock variability of the means, represented as cumulative distributions for the consecutive stages of processing until cutting (red line at the lower end).
The variability is large and does not decrease. L2 = input, M2=scalding, etc. until cutting (=S2).

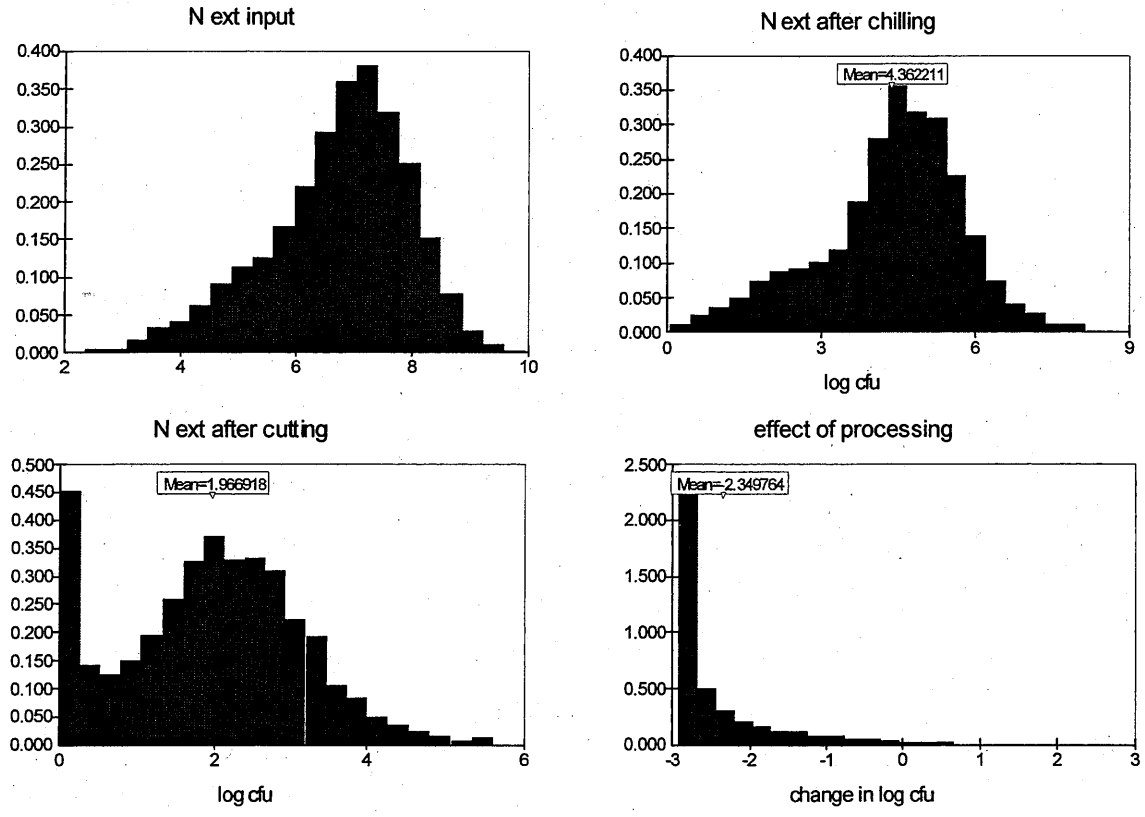

Figure 4.6 Between-flock distributions of the means per flock of log($N_{ext,\ input}$), log($N_{ext,\ chilling}$) and log($N_{ext\ cutting}$) and the effect of processing until chilling.
The small value (left hand) tail of the upper graphs results from the flocks with low animal prevalence. The effect of processing is a skewed distribution. The tail in the effect of processing is a consequence of flocks where C_{fec} is large and N_{ext} is low. Here, cross-contamination by faeces yields higher levels at the exteriors, up to values higher than $N_{ext,\ input}$.

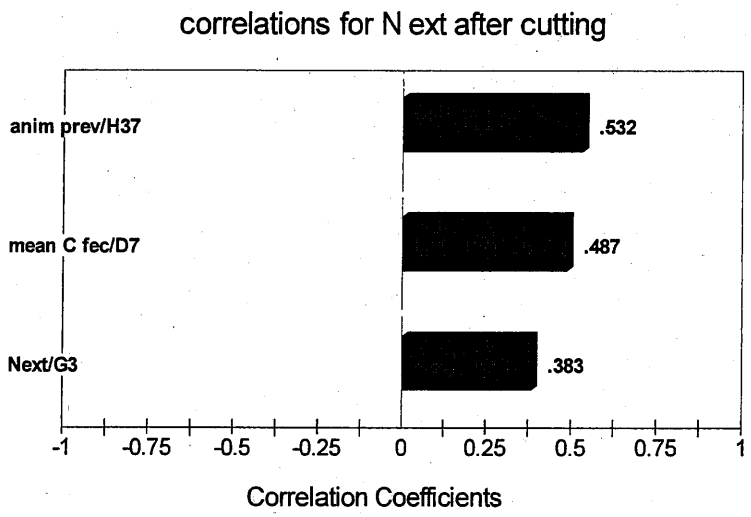

Figure 4.7 The results of a sensitivity analysis in @Risk, in which the output distribution of the mean of $N_{ext,\ cutting}$, is correlated with the input distributions of P_{anim} , $N_{ext,input}$ and C_{fec} by rank correlation.

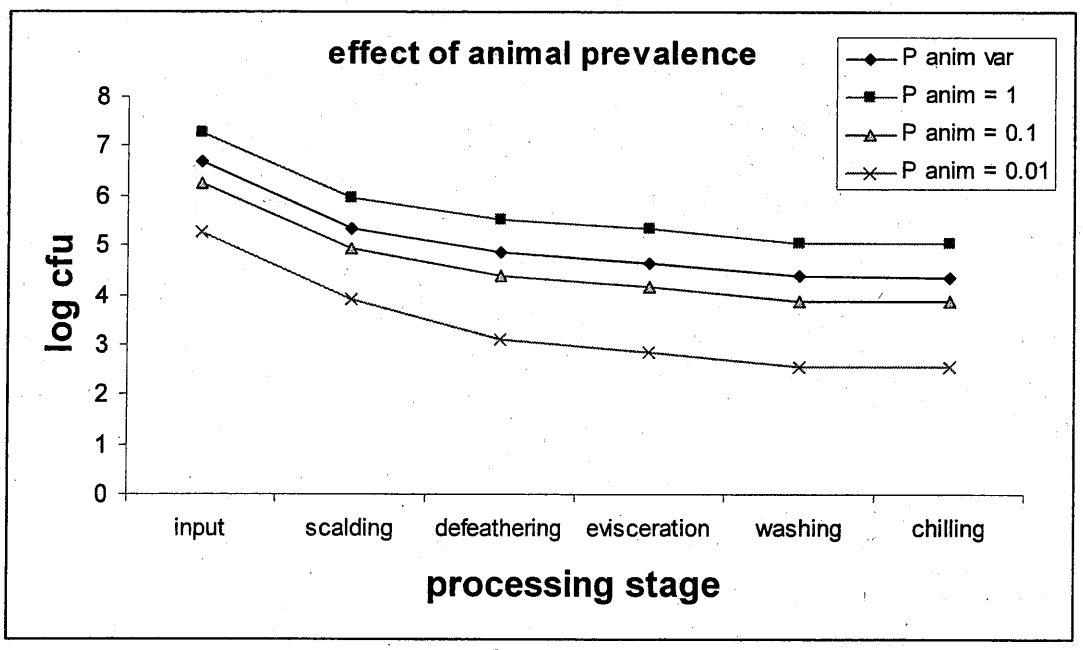

Figure 4.8 The effect of animal prevalence on the change in log (N_{ext}) during processing. In the baseline P_{anim} varies between processed flocks.
The mean result is a combination of results of flocks with high and low prevalence. For comparison, the mean results are shown of the baseline model with fixed values for P_{anim}.

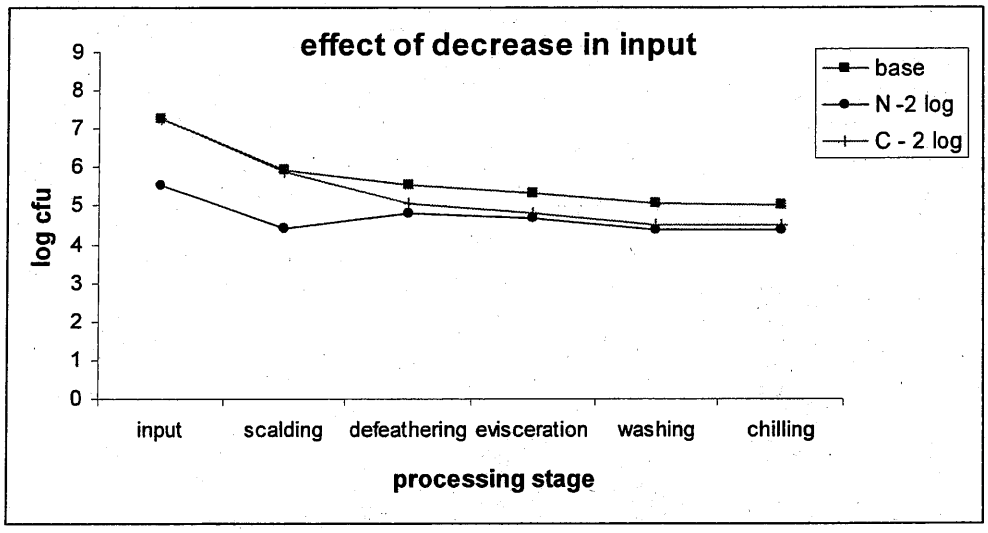

Figure 4.9 Results for the mean effect of processing in the baseline model with animal prevalence P_{anim} = 100% (base) and modified mean values of log (N_{ext}) and log (C_{fec}). Both the mean of N_{ext} and C_{fec} are decreased by two log units.

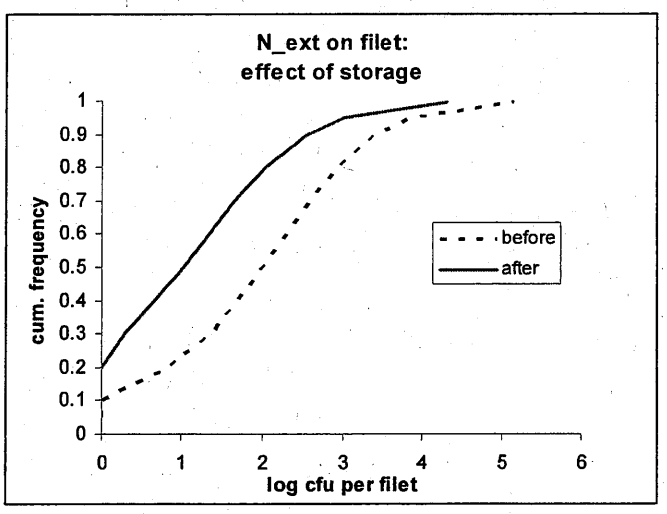

Figure 4.10. The modelled effect on log(N_{ext}) of storage of chicken breast fillets in the refrigerator.

After cutting and deboning, within-flock dynamics are no longer relevant and fillets are randomly sampled from the 5000 flocks simulated in the processing model. Hence, within-flock variability and between-flock variability can be combined. Fig 4.10 shows the effect of storage on the distribution of N_{ext}, the number of campylobacters on the fillets. Note that these are only fillets of chickens from contaminated flocks.

Finally, as an effect of food handling, the distribution of $N_{consumption}$ is once more shifted to lower numbers of campylobacter. For adults and young, the predicted frequency of exposure to campylobacter is in resp. 0.81% and 0.67% of the meals with chicken breast fillet and salad. For the whole population the prevalence of contaminated salad portions is estimated to be 0.80%.

The distribution of the numbers ingested is illustrated in fig 4.11. It can be seen that the majority of exposures is to doses of 1 and 2 cfu. Less than 2% of the exposures is to doses > 100 cfu campylobacter.

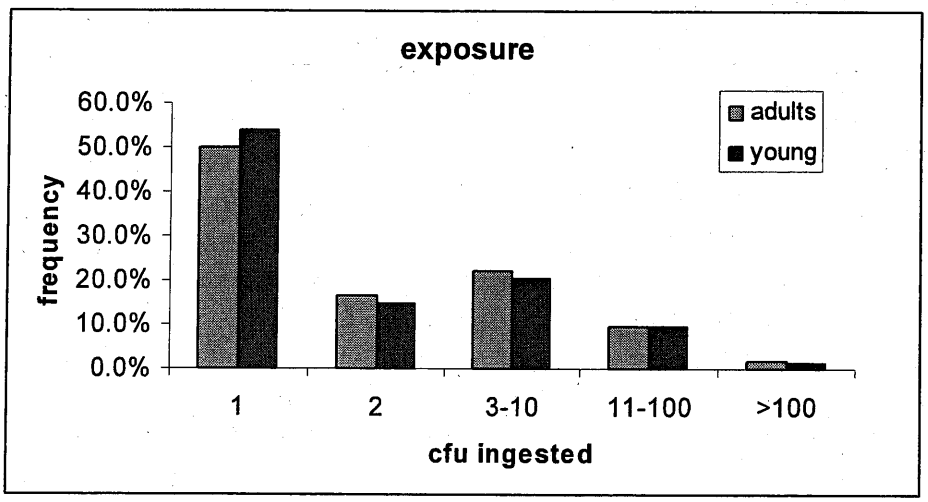

Figure 4.11 The predicted frequency distribution of ingested doses of campylobacter resulting from the baseline risk model.
These exposures occur in 0.81% (adults) and 0.67 % (young) of the meals considered in the assessment.

In the end the baseline model predicts 12,327 cases if the classic dose-response model is applied and 170,136 cases if the new model (Teunis et al. 2005) is applied. In the latter model it is predicted that 17.84% of the cases are young people (14 years and younger).
These numbers seem to be high estimates, being the cases of campylobacteriosis predicted per year in the Netherlands as the consequence of the consumption of salad prepared together with chicken breast fillet only. This is larger than expected on the basis of epidemiology.
The relative frequency of the different dose classes as shown in fig 4.11 can be compared to the percentage of human cases attributable to exposure to that dose class. This is shown in table 4.2 and fig 4.12. Although 11.5% of the exposures is to doses > 10 cfu, 45.4% of the human cases is attributable to these exposures.

Table 4.2 The ingested doses and their effects.
For five classes of doses the table shows: the relative frequency (% exposures); the probability of infection given this dose; the probability of infection given exposure (= the product of the previous two columns); the relative frequency of cases attributable to the dose class (= the relative frequency of the previous column).

dose (cfu ingested)	% exposures	$P_{inf\|dose}$	P_{inf}	% cases
1	50.1%	1.9%	1.0%	16.5%
2	16.3%	3.5%	0.6%	10.0%
3-10	22.2%	7.2%	1.6%	28.1%
11-100	9.7%	19.5%	1.9%	33.2%
>100	1.8%	39.1%	0.7%	12.2%

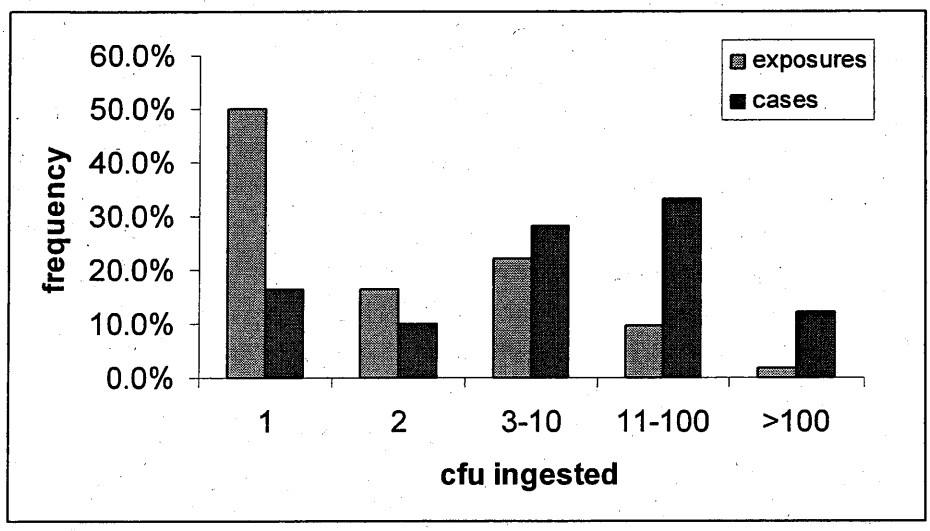

Figure 4.12 The relative frequencies of dose classes and the percentages of human cases of campylobacteriosis attributable to those classes.
Higher doses have more impact than the distribution of exposures suggests.

In the analysis of the effects of interventions we focus on the relative risk and the relative risk reduction. Here the relative risk is defined as the ratio between the number of cases predicted after intervention, divided by the number of cases predicted in the baseline. Unless otherwise stated we apply the classic model, which seems to yield a more realistic prediction of the incidence of human cases.

4.2 Interventions

A comparative overview of the results of the interventions is given in fig 4.13 and table 4.3.

4.2.1 Farm

A comparison of the predicted risk reduction (= 100% - relative risk) of interventions at the farm, shows that applying phage therapy has the largest effect.
- For thinning we could not evaluate the effect of a ban on thinning practices: as this practice was not specifically incorporated into the baseline farm model, it could not be left out either. The opposite, however, the effect of thinning at all farms, could be modelled by incorporating the introduction of campylobacters at all farms about a week before slaughter. This mirrors the effect of a ban on thinning and the result is an increase of the relative risk (>100%). As in this case time is too short for campylobacter to spread through the farm, this yields many infected flocks with very low animal prevalence. Although it is assumed that all birds in colonized flocks are contaminated on their exterior (see sections 3.2.2. and 3.3.3.), the model shows that these low prevalent flocks have very little effect on the final risk. As confirmed by the alternative scenario analysis (see section 4.3.1), the effect of a low prevalence of

colonized birds sufficiently lowers the human exposure. Overall, this gives a good argument for the statement that thinning will not be a significant risk factor.

- The predicted effect of improved hygiene at the farm is quite uncertain, mainly because there are little data that show how the effects of hygiene can be quantified. The 10% effect as implemented is a 10% reduction of the transmission coefficients in the farm model (Katsma et al. 2005) and is considered to yield the most likely value for this intervention. Pessimistic and optimistic effects are 5% and 25% effect, respectively. The 10% effect can also be split in a 10% decrease of the within-production cycle transmission coefficient only and a 10% decrease of the between-production cycle transmission coefficient only (which add up to the total 10% effect; see Katsma et al. (2005) for details). This shows that 25% of the risk reduction achievable by this intervention can be obtained by lowering within-production cycle transmission and 75% by lowering between-production cycle transmission.
- Phage therapy lowers the concentration of campylobacter in the faeces (C_{fec}) by two logs, and this has considerable effect (about 75% risk reduction).

Table 4.3 The estimated effects of interventions.
Columns show the risks relative to the baseline model, the prevalence of contaminated fillets after cutting (for fillets from birds from contaminated flocks), the mean log number of campylobacters per contaminated fillet after cutting, and the risk reductions without (all) and with scheduled treatment (using dipstick, PCR and culture test methods) as shown in fig 4.13.
* prepared meat without scheduled treatment is not a reasonable intervention, the results is given for comparison

				risk reduction			
	relative risk	prevalence after cutting	mean log $N_{ext,cutting}$	all	dipstick	PCR	culture
home freezing	99.1%	94%	1.97	0.9%			
kitchen hygiene	96.5%	94%	1.97	3.4%			
prepared meat	0.0%	-	-	100.0%*	78.2%	87.0%	66.6%
product freezing	5.1%	76%	0.64	94.9%	74.0%	82.3%	63.0%
irradiation	0.0%	0%	-	100.0%	78.2%	87.0%	66.6%
crust freezing	17.2%	85%	1.08	82.8%	65.2%	72.1%	55.4%
decont. 3x TSP	9.4%	80%	0.87	90.6%	71.4%	79.2%	60.8%
decont. 3x lactate	7.9%	77%	0.70	92.1%	71.8%	79.9%	61.0%
decont. 1x TSP	13.1%	83%	0.98	86.9%	68.2%	75.4%	57.7%
decont. 1x lactate	12.1%	83%	0.94	87.9%	69.1%	76.6%	58.8%
scald tank TSP	82.0%	89%	1.57	18.%			
scald tank lactate	87.6%	90%	1.64	12.4%			
faecal leakage	22.9%	91%	1.48	77.1%			
phage therapy	25.6%	92%	1.54	74.4%	57.5%	63.3%	48.3%
farm hygiene	57.1%	94%	1.92	42.9%			
always thinning	101.3%	-	1.97	-1.3%			
baseline	100%	94%	1.97	0%			

4.2.2 Scheduled treatment

With scheduled treatment flocks are tested for the presence of Campylobactre before slaughter, and positively tested flocks are treated by an intervention. The difference with logistic slaughter is that the order of processing flocks at a processing plant need not be changed. Negatively tested flocks are treated as usual, and with parameter values as

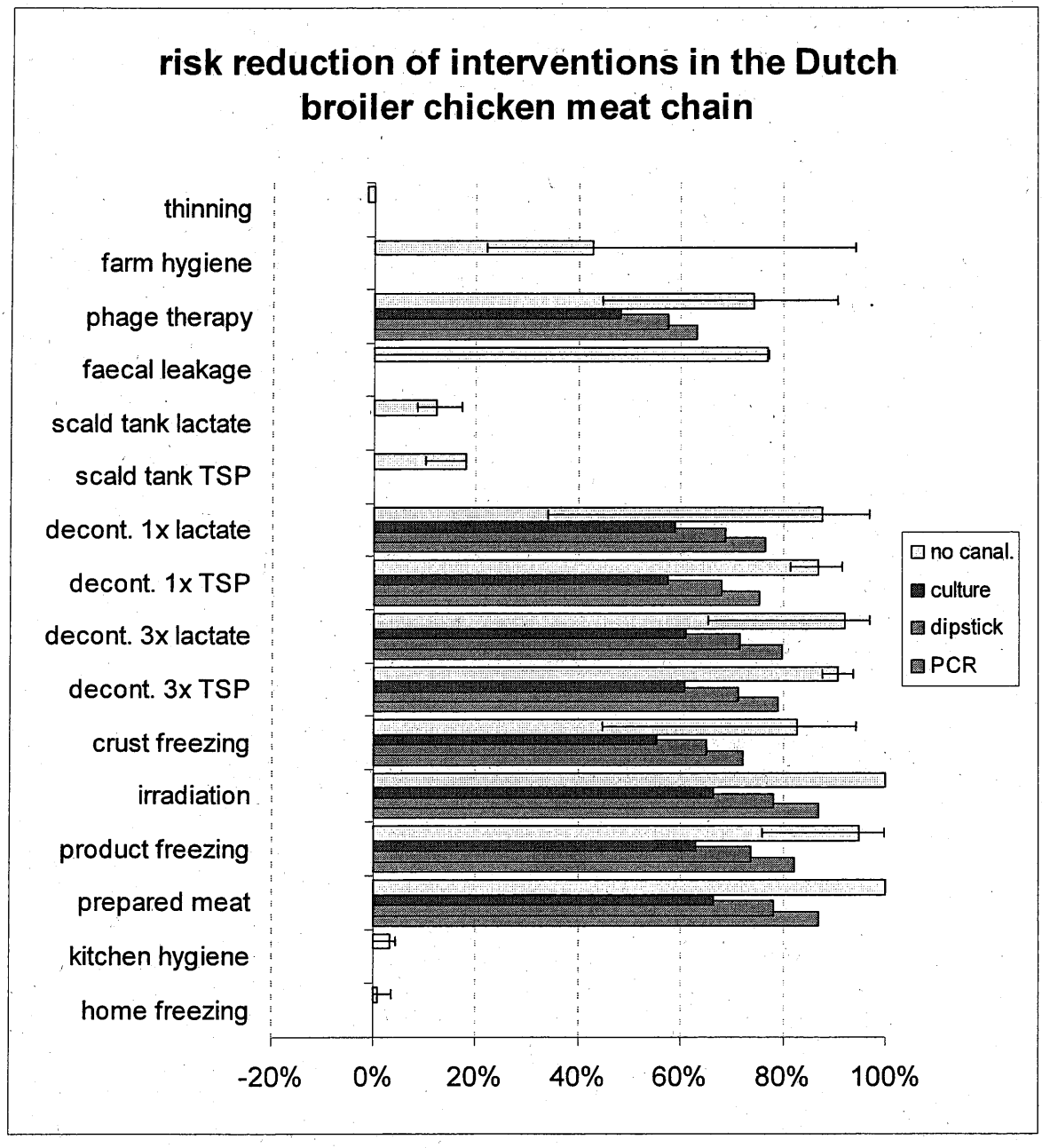

Figure 4.13 The predicted risk reduction as a consequence of the interventions.
The risk reduction is 100% minus the relative risk of each intervention, and stands for the percentage of cases of campylobacteriosis due to the consumption of Dutch chicken meat saved by implementation of this intervention. Yellow bars show the result without scheduled treatment, with error bars expressing an uncertainty interval that results from using pessimistic and optimistic interpretation of the effects of the interventions. The other bars show the effects with scheduled treatment, using culture, dipstick and PCR resp. as testing method at the farm.

applied in the baseline. Due to a limited sample size of tested birds in a flock (we assume a sample size of 10) and a test sensitivity smaller than 100%, these negatively tested flocks still hold (false negative) infected flocks, which may lead to chicken meat contaminated by campylobacter. These false negative flocks in general hold many flocks with low animal prevalence.
The maximum risk reduction can be achieved by elimination of positive flocks from the fresh meat production chain, for example by giving heat treatment to the chicken meat products from positively tested flocks to produce prepared meat. These maximum effects are shown in fig 4.14 and table 4.4. The PCR test seems to be the best testing method due to the highest sensitivity, and despite the longer time needed between test and test result. The dipstick is second best and the traditional culture methods show the least risk reduction. No matter which test will be used, there will always be false negative flocks, due to the limited sample size. When the animal prevalence is low no reasonable sample size is sufficient to detect these low prevalence flocks.

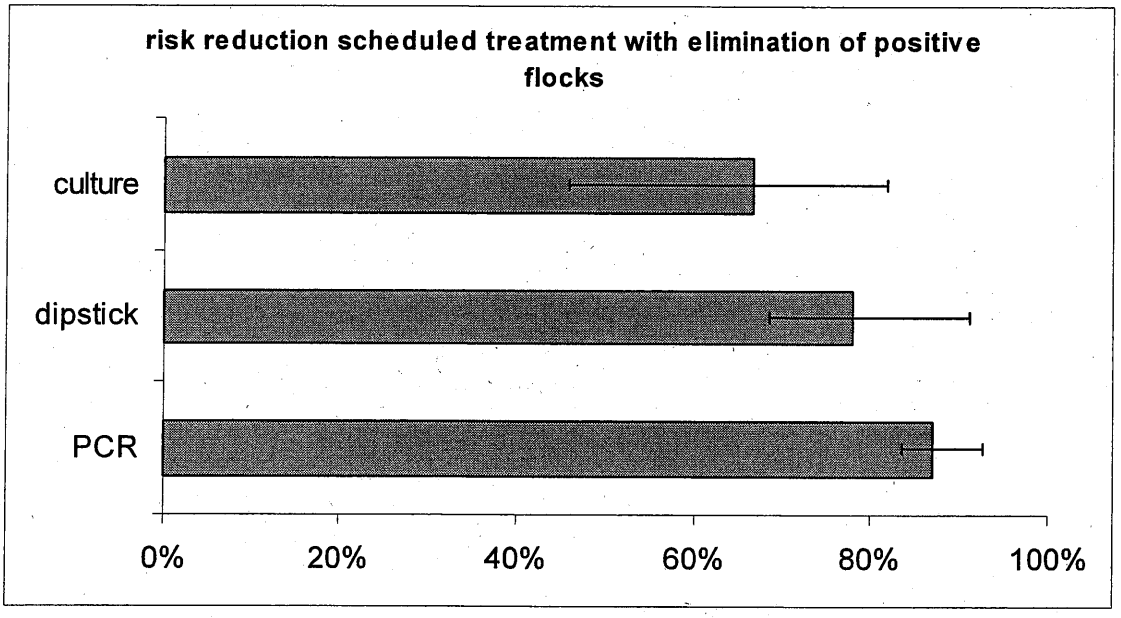

Figure 4.14 Maximum risk reduction that may be achieved by scheduled treatment.
The uncertainty in effects of scheduled treatment given by the confidence bars are a consequence of uncertainty in the test sensitivities. The risk reduction is shown when positive tested flocks are eliminated from the fresh food production chain (e.g. by heat treatment).

4.2.3 Processing

Interventions during processing are all aimed at the contamination of the carcass (or chicken product) exterior, except the intervention aimed at lowering faecal leakage.
The latter may be quite effective, although this effect is rather uncertain. Decontamination of the exterior gets more effective further down the processing chain. Decontamination at the scalding stage is not very effective, as contamination with faeces can still occur after that stage. After evisceration cross-contamination by faeces will no longer occur, which makes decontamination more effective.

Table 4.4 The estimated effects of scheduled treatment applying different test methods.
Here it is assumed that with scheduled treatment all positively tested flocks are processed as prepared meat. The relative risk compared to the baseline is a result of false negative (=negatively tested but colonized) flocks. In bold are the results for the most likely sensitivity and specificity of the tests. Alternatives have different sensitivity and/or specificity. Differences between methods in results with 100% sensitivity and 100% specificity are caused by a difference in time span between testing and slaughter. The sample size for each test is 10 birds. The percentage of false negative flocks (last column) is the percentage of all processed flocks that are colonized but tested as negative.

	sensitivity	specificity	relative risk	risk reduction	false neg. flocks
dipstick low	70%	95%	31.3%	68.7%	21.3%
dipstick	**80%**	**95%**	**21.8%**	**78.2%**	**18.1%**
dipstick high	95%	95%	8.8%	91.2%	13.2%
dipstick best	100%	100%	3.7%	96.3%	12.3%
dipst. low spec	80%	80%	21.6%	78.4%	16.2%
PCR low	90%	100%	16.4%	83.6%	17.2%
PCR	**95%**	**100%**	**13.0%**	**87.0%**	**15.7%**
PCR high/best	100%	100%	7.4%	92.6%	14.2%
PCR low spec	95%	90%	12.7%	87.3%	14.3%
culture low	50%	90%	54.2%	45.8%	28.7%
culture	**75%**	**90%**	**33.4%**	**66.6%**	**21.7%**
culture high	90%	90%	18.1%	81.9%	17.5%
culture best	100%	100%	13.2%	86.8%	16.3%
cult. high spec	75%	100%	34.2%	65.8%	23.3%

Results also show that the effect of decontamination of the carcasses with TSP seems to be less uncertain than the effect of lactate, but this may partly be due to the scarcity of data. Decontamination at three stages during processing is more effective than decontamination before chilling only. However, the difference in the predicted effect is rather small.
The effect of crust freezing may be smaller than the effect of decontamination, but still gives a risk reduction of more than 80%.
Finally, as expected, irradiation, product freezing and the production of prepared meat are very effective in reducing the relative risk.

4.2.4 Consumer

The effect of interventions at the consumer stage is expected to be small, mainly because these effects are based on the presumed limited effects of information campaigns. As stated, the effect of these campaigns on the actual behaviour of the public are hard to predict, largely depending on the precise implementation of these campaigns. Therefore the uncertainty bounds are quite imprecise. For freezing, the assumed duration of frozen storage has far less impact on the risk reduction than the effect of the information campaign. If people would store the product for two weeks instead of two days the risk reduction increases to 3%.

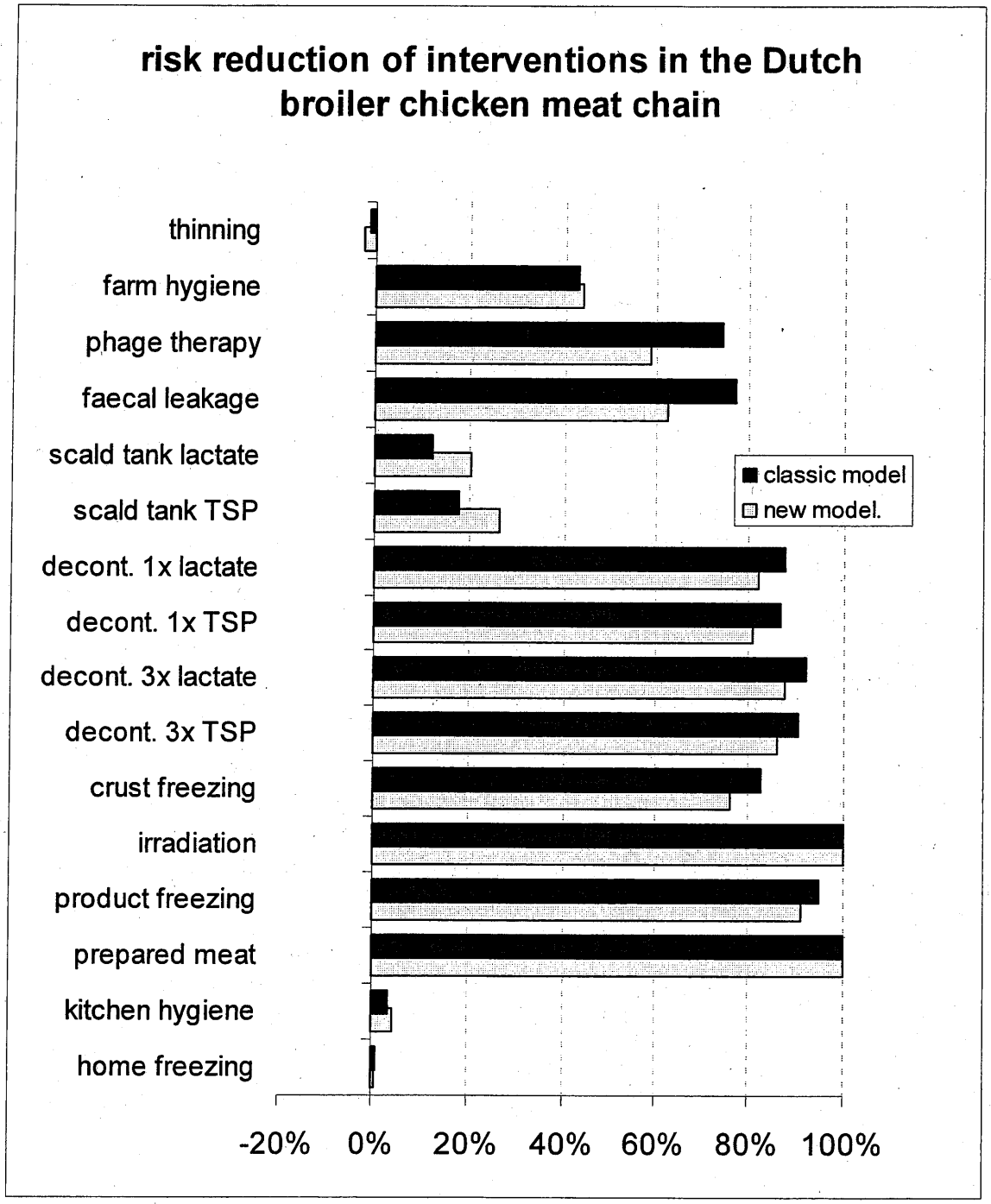

Figure 4.15. Comparison of the predicted risk reductions with application of the classic dose-response model and the new dose-response model (Teunis et al. 2005). Roughly, effects are similar, but differences exist for example when intervention aim at either the carcass exterior, or the level of colonization in early stages of processing. These differences are to be explained by a change in the shape of the distribution of exposures.

4.2.5 Comparison of response measures

In the baseline model we apply the classic dose-response model (Teunis and Havelaar 2000).

With the new dose-response model (Teunis et al. 2005) the predicted numbers of cases are much higher, but the effects of interventions in terms of risk reduction are similar. This is illustrated in fig 4.15, which shows that for most interventions a larger risk reduction is predicted, but not for the decontamination of the scalding tank. Reason for this must be the effect on the shape of the exposure distribution as a consequence of targeting N_{ext} when the carcass still holds its intestines.
When the new dose-response model is applied, we are able to differentiate between the cases of young (14 years and younger) and adults (15 and older), assuming the first group is more sensitive to campylobacter than the second (See section 3.2.7 and fig 4.16.) The percentage of cases of each group varies for the different interventions, but only to a small extent (between 14.4 and 18.4%).

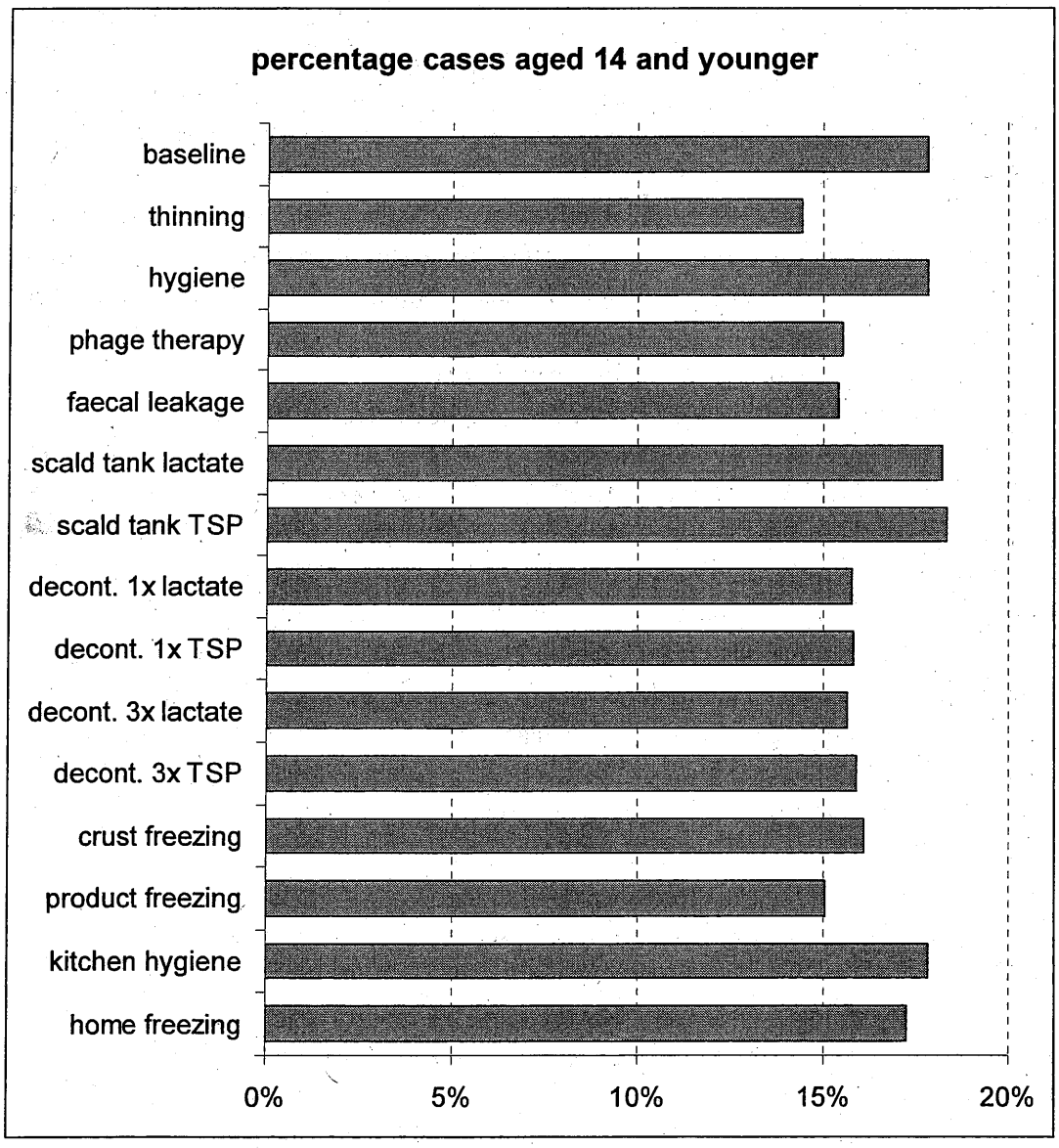

Figure 4.16 The percentage of cases attributable to the young (14 years and younger) for the intervention scenarios and the baseline study.

4.3 Alternative scenarios

An overview of the effects of the alternative scenarios on the relative risk as calculated with the risk model is given in fig 4.17.

4.3.1 Input N_{ext} and C_{fec}

- In the baseline risk model $N_{ext,\ input}$ and C_{fec} are sampled independently. This implies that for bird/carcass i the level of contamination on the exterior and the concentration in the faeces are not correlated. This assumption may be doubted. When the model was run with 90% correlation between the two, however, the effect on the relative risk was small (3% lower risk with the classic dose-response model, the model used for evaluation unless stated otherwise.)
- It is assumed in the baseline that all birds in flocks with at least one colonized bird are contaminated on their exterior due to cross-contamination between the faeces and exteriors of the birds during rearing and transport. This may not be realistic in low prevalent flocks.
To study the impact of this assumption, we also ran the baseline model assuming that only colonized birds are contaminated on their exterior, omitting the correction for low prevalence in the baseline (see 3.3.3). In this case the relative risk is 3% lower, so it is almost identical to the baseline and it can be concluded that the effect of this assumption is negligible. The reason for this is that the total amount of campylobacters introduced in the system at the input remains equal.
- Lowering $N_{ext,\ input}$ to zero, or by one log unit, has little impact on the relative risk. (20-10% lower risk, to 80 and 90%) An increase by one log unit, however, doubles the risk.
- Lowering C_{fec} to zero, or with two log units or more, all has an effect of about 75% lower risk, yielding relative risk 25%. (See also the effect of the intervention 'reduction of faecal leakage'.) A decrease with 1 log unit still gives relative risk 40%. An increase with 1 log unit triples the risk.
Adding of the results for $N_{ext,\ input}$=0 and C_{fec}=0 yields 12891 cases, 105% of the baseline. A comparison of the two sources shows that about 22% of the cases result from campylobacters that are on the birds exteriors at the entrance of the processing plant and 78% from campylobacters in the leaking faeces. Hence the campylobacters in the faeces are predicted to be the dominant source.
In this context it is interesting to have a closer look at the results for the scenarios $N_{ext,\ input}$=0 and C_{fec}=0. The results of a comparison of the mean and 5, 50 and 95 percentiles of the between-flock distributions of the means per flock of log $N_{ext,\ chill}$ and log $N_{ext,\ f}$ are illustrated in fig 4.18. It shows that most frequently the campylobacters on the exterior at the entrance of processing are the main source of campylobacter: the geometric mean of the numbers and the median are larger for the C_{fec}=0 scenario. However, the variability in the numbers originating from leaking faeces is much larger. The 95 percentile for the $N_{ext,\ input}$=0 scenario is higher than the same percentile for the other scenario. This upper tail of the distribution is most important for the final health risk and thus determines the finding that most human cases of campylobacteriosis are predicted to result from campylobacters in the birds intestines at the entrance of the processing plant.

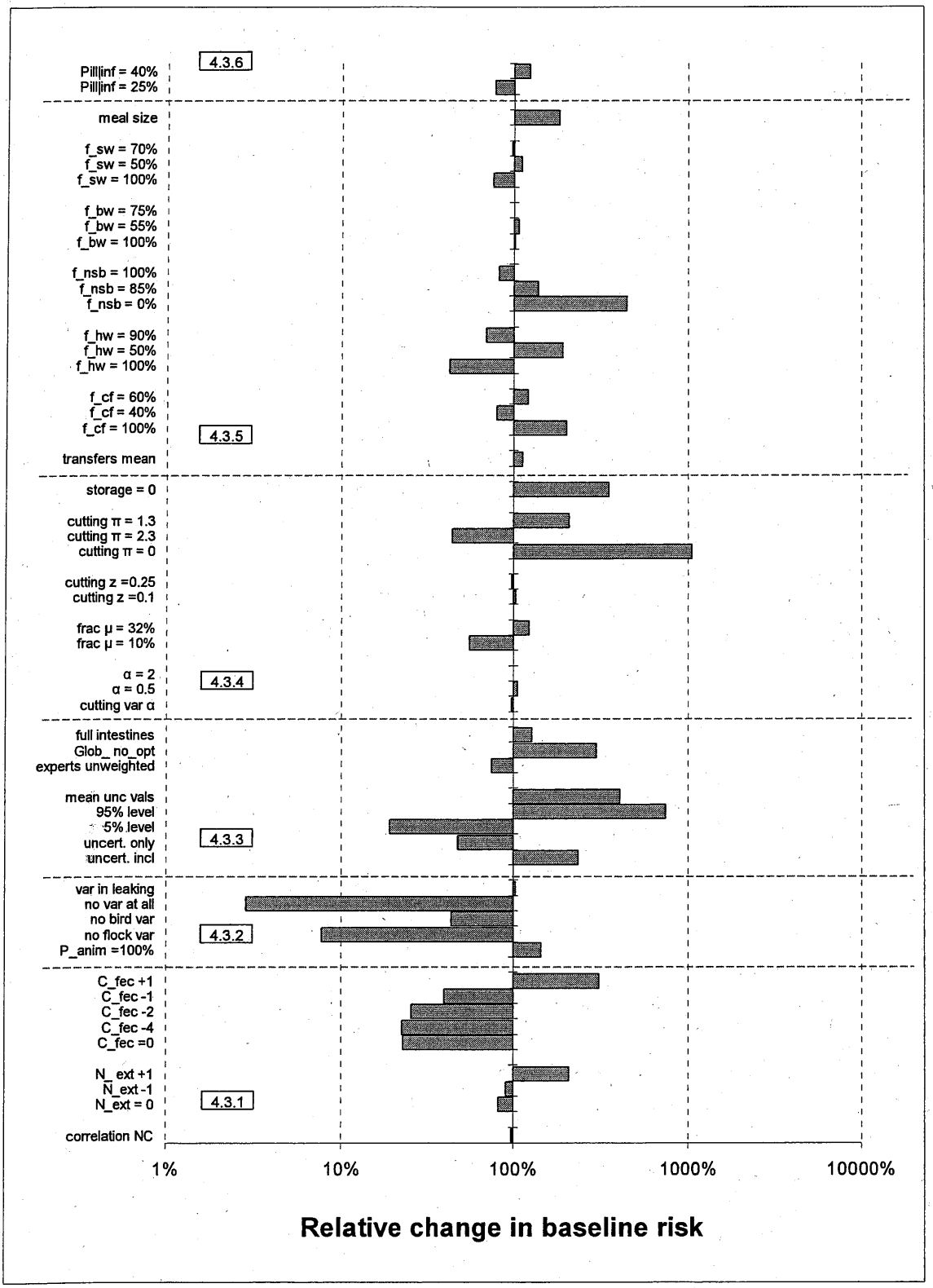

Figure 4.17. Risks as calculated with alternative scenarios, relative to the baseline risk estimate (=100%).

The bars give the results per scenario for the classic dose-response model. Note the log scale at the x-axis. Results and abbreviations are discussed in the main text, in the sections mentioned in the boxes.

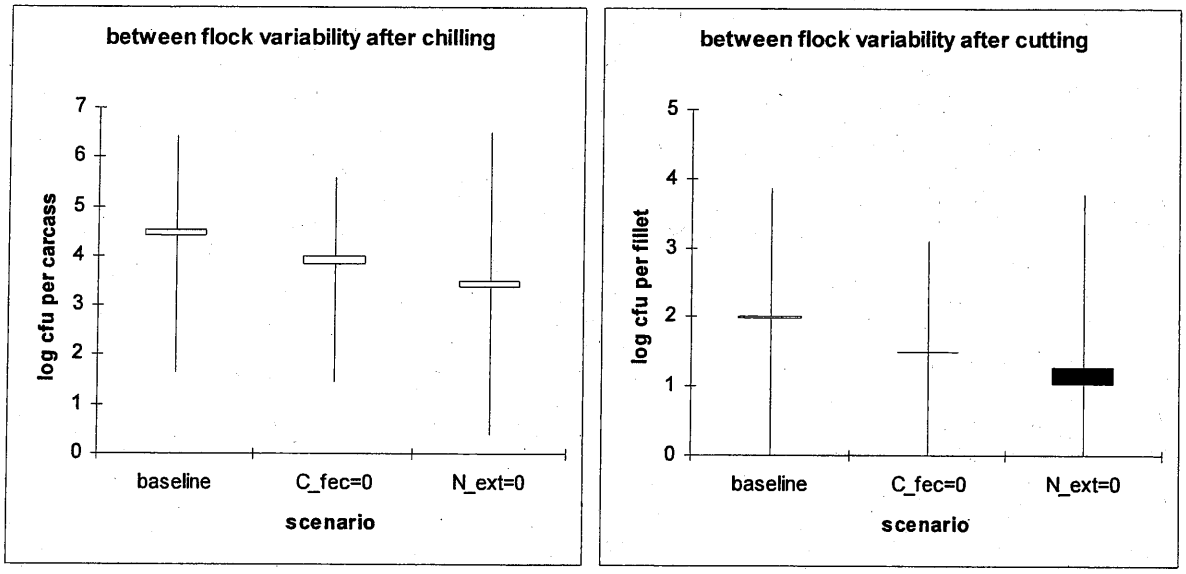

Figure 4.18 Comparison of the birds exterior and their intestines as source of campylobacter on the meat.
The variability in mean results per flock are compared for the baseline and the alternatives $N_{ext,\,input}$ =0 and C_{fec} = 0 for all birds in the flock. The boxes indicate the mean and the median, bars give the range between 5 and 95 percentiles. If the mean is smaller than the median the box is white, else it is black. The graph left shows the result for log $N_{ext,\,chill}$, right for log $N_{ext,\,f}$. Central values for the C_{fec} = 0 scenario are larger, but the 95% is lower. The latter has most impact on human exposure and the associated health risk.

4.3.2 Variability between birds and flocks

- When differences in the animal prevalence are omitted and the prevalence is set at 100% in all flocks, this yields a higher relative risk (increase to 140%). This is not unexpected because more contaminated animals are introduced.
- If the variability in $N_{ext,input}$ and C_{fec} between flocks and/or the variability between birds is omitted, by setting the matching standard deviations at zero, the relative risk decreases dramatically (to 8%, 45%, 3% for between-flock, between bird and both.). The reason for this that the distributions for $N_{ext,input}$ and C_{fec} are lognormal, so that the arithmetic mean is decreased when the standard deviation is decreased.
- When the variability between birds in the amounts of leaking faeces ($m_{s\,\sigma}$) is increased (standard deviation is 0.5 instead of 0.001) the effect is negligible.

These results show that taking variability between flocks and between birds into account is essential for the model. However, variability in amounts of leaking faeces could just as well have been omitted from the model. An important factor here is the fact that for $N_{ext,input}$ and C_{fec} we assume a lognormal distribution, and a normal distribution for m_s.

4.3.3 Processing model and expert study uncertainty

The uncertainty in the processing model parameters has been studied extensively in the formal expert judgement study (Van der Fels-Klerx et al. 2005). However, we were not able to integrate this uncertainty in the final baseline risk model, because this would require a third

order Monte Carlo, incorporating two levels of variability and this uncertainty additional to that. We were not able to do that with the available research facilities. The impact of the uncertainty could however be explored by running the model with some alternative scenarios.
- If the uncertainty in the model parameters is included as if it were variability between flocks, the relative risk increases to about 235%. Reason for this effect is that the tails of the distributions get larger, due to an increased variance. The right hand tail, with large values for levels of contamination etc., is dominant in determining the final risk.
- If the between-flock variability is excluded, by setting P_{anim} = 100% and setting the between-flock standard deviation of $N_{ext,input}$ and C_{fec} at zero, and the uncertainty of the processing model parameters as derived in the expert study (Van der Fels-Klerx et al., 2005) is taken into account, the change in relative risk is not informative. However, other model results give relevant insight of the impact of this uncertainty. This is illustrated in fig 4.19 to 4.22.

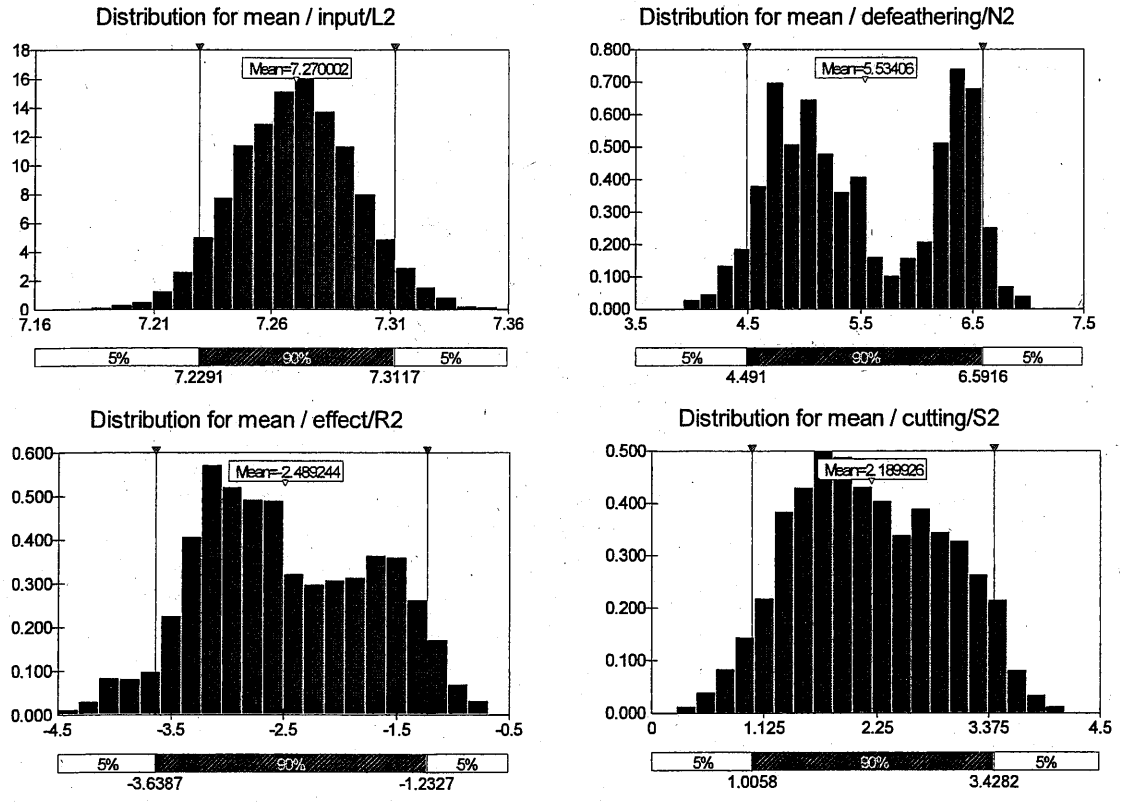

Figure 4.19. Uncertainty distributions of the mean levels of N_{ext} per flock, in 5000 simulation runs of the risk model without between-flock variability, but with uncertainty in the processing model parameters.
Distributions of N_{ext} are shown for the input, after defeathering, the effect of processing (until chilling) and after cutting. The uncertainty increases down the processing chain. Note the bimodal distributions after defeathering, caused by the bimodal shape of the uncertainty of parameter $b_{env, def}$ (see fig 4.22). The bar at the bottom shows the central 90% percentiles.

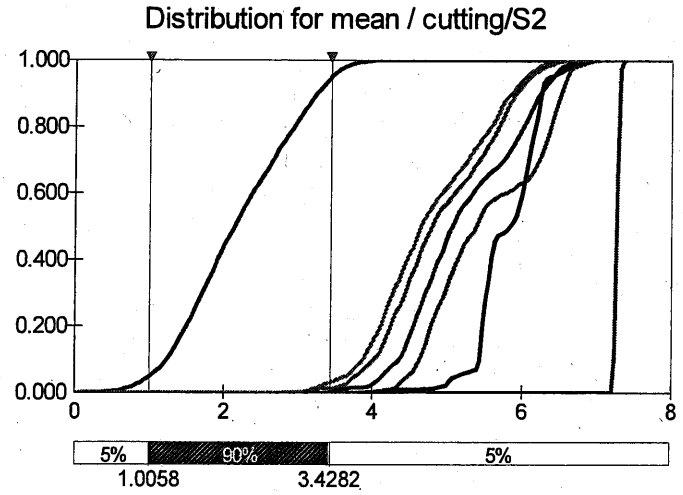

Figure 4.20. The cumulative uncertainty distributions of log (N_{ext}) (from right to left) at the input and after scalding (black line), defeathering, evisceration, washing, chilling and cutting.
The bimodal shape of the distribution is illustrated by the shoulder in the curves.

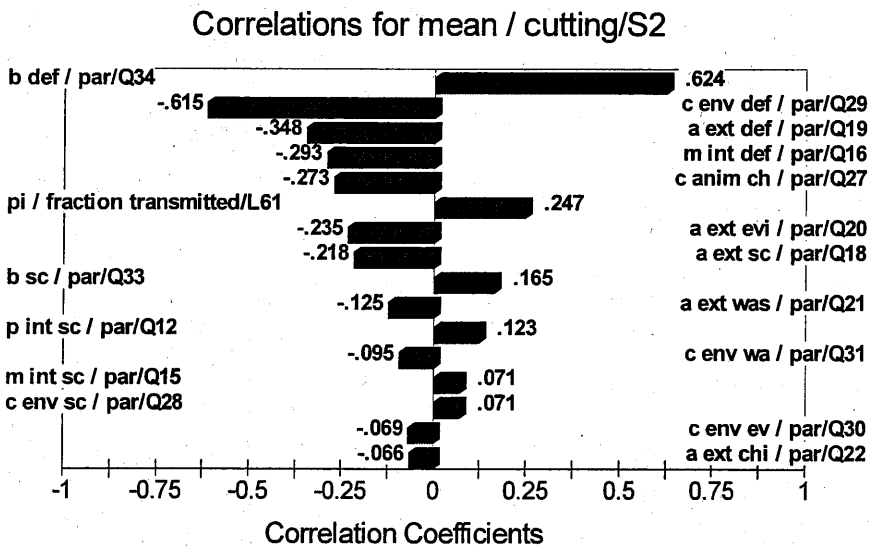

Figure 4.21. The results of a sensitivity analysis in @Risk, in which the output distribution of the mean of $N_{ext,\ cutting}$, is correlated with the input distributions of the processing model parameters.
It shows that the uncertainty of estimates at the defeathering (def) stage has the largest effect on the uncertainty in the level after cutting. The fraction transmitted with cutting, π (indicated by pi), can also be found higher up in the list.

From the tornado chart with correlations between input and output (fig 4.21; the level of campylobacter on carcasses after cutting) it can be seen that this output is most sensitive to the uncertainty in the parameters for the defeathering stage, with on top the parameter $b_{env,\ def}$, describing the probability per cfu campylobacter in the environment during defeathering to

move to the carcass. As a result of the probablistic inversion (Cooke et al. 2004) on the parameter estimates, the uncertainty of this parameter appears to be bimodal. As illustrated in fig 4.19 this bimodality is expressed in the distribution of the mean level per flock after defeathering, and to a lesser extent in the distributions of the effect of processing and the level after cutting.

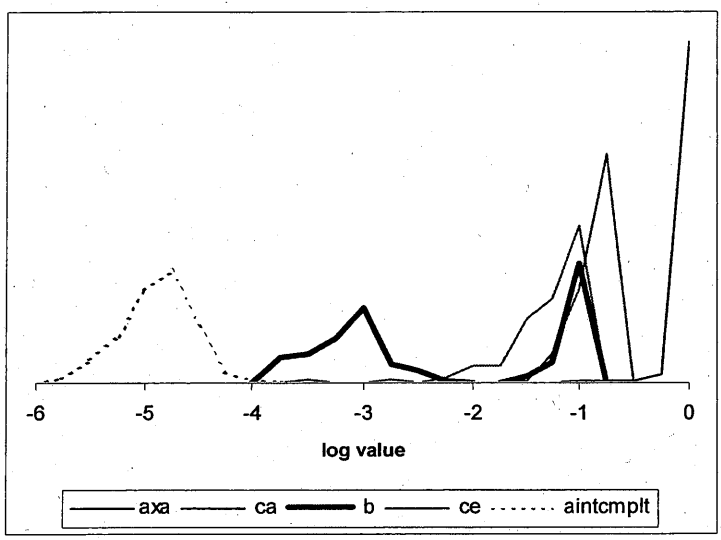

Figure 4.22 The uncertainty distribution of the processing parameters a_{ext} (axa) c_{ext} (ca), b_{env} (b), c_{env} (ce), and 1- a_{fec} (aintcmplt) for the defeathering process, resulting from the probablistic inversion on the expert estimates.
Note that the uncertainty distribution of b_{env} is bimodal.

- Analysis of the results of model runs where the uncertainty is included show that the 5% and 95% percentiles of the uncertainty distribution show a decrease of about 1 log unit and an increase of about 1.5 log unit in the mean value of N_{ext} after cutting. To get an impression of the uncertainty in the estimates of the baseline risk as a consequence of the uncertainty in processing model parameters, the model is run by subtracting 1 log unit to the level N_{ext} after cutting and adding 1.5 log unit after cutting. This is a rather rough method to explore the uncertainty about the estimate of 12327 cases as a consequence of the effects of industrial processing. It yields relative risks of 19% and 740% respectively, illustrating that the range of this uncertainty is large.
- In the baseline model analysis we use the median values of the processing model parameters. This choice was made because the uncertainty distributions may be quite skewed. The model was also run with mean values instead of median values. This yielded a relative risk of 400%.
- The 'best' decision maker that resulted from the calibration and weighing of experts in the expert study was the 'global optimized decision maker' (see Van der Fels-Klerx et al. (2005)). We therefore analyzed the model with the median estimates for two other decision makers considered: one where the weighing of experts was omitted and another one where a global non-optimized decision maker was taken (in which more weighted experts are included than for the global optimized decision maker). This results in a decrease (to 75%)

and increase (to 300%) of the relative risk, again illustrating that the end result of the model depends on some subjective assumptions.
- Also, in the baseline the choice was made to use the expert estimates for 'half full' intestines of the (usually to some extent fastened) birds entering the processing plant. This is one of the two alternatives for which expert were elicited in the expert study, the (less common) alternative being flocks with 'full intestines'. Birds in such flocks are not fastened and are therefore expected to leak higher amounts of faeces during processing. Using expert estimates for 'full intestines' has little impact (relative risk 130%). This is in contradiction to the observed impact of the reduction of faecal leakage (see 4.2.3). The discrepancy may be due to the complexity of this issue and the underlying assumptions of the consulted experts.

4.3.4 Cutting and storage

- For the partitioning model at the cutting stage we studied the effect of changes in α_1, a parameter of the Beta distribution Beta(α_1,α_2) describing the variability of probability p_{cut}, and μ, the mean value of p_{cut} . The impact of changes in α_1 (by either taking a lower or large value, or taking it as a variable) is negligible. We could have chosen a Binomial distribution with fixed probability for the partitioning process instead of a Betabinomial distribution (Nauta 2005). The mean value of p_{cut} (baseline 24%) is set at a lower and upper bound as discussed in section 3.2.3. The lower (10%) yields a relative risk of 55%, the upper bound (32%) yields a relative risk of 125%.
- Cross-contamination parameters are studied by analyzing the effect of changes in parameters z (the percentage of the campylobacter contamination on the fillet directly originating from the breast cap that it is cut from) and - log π (the estimated -log of the fraction transmitted from breast cap to double fillet). Changes in z have little impact, but the impact in changes in π may be larger. If we take log $\pi = 0$, as concluded by Berrang et al. (2001), we get the highest relative risk in the alternative scenario analysis, > 1000%. Values closer to the (uncertain) value adapted in this study, based on Dutch expert guesses, this still has a considerable impact on the end result (- log $\pi = 2.3$, relative risk 44%; -log $\pi = 1.3$, relative risk 200%)
- For the storage effect we apply data recently collected for the CARMA project, showing that storage at refrigeration temperature leads to a decrease in the level of campylobacter on chicken breast fillet. If this (uncertain) effect is neglected, the relative risk increases to 350%.

4.3.5 Consumer food handling

- For the food handling processes, we modified the values of the frequencies in which certain handling are performed by the consumers. It shows that if every consumer cooking a chicken meal washes her/his hands, the relative risk lowers to 43%. If 90% washes hands instead of 80%, it decreases to 70%. The impact of frequency changes in other practices modelled is smaller. Note that we could not find any data on the frequency in which chicken is prepared before the salad, and that this frequency is linearly related to the incidence of campylobacteriosis due to the modelled salads. A thorough sensitivity analysis of the

consumer food handling model is presented in Mylius et al. (submitted), who concluded that it might be better to aim an information campaign at board washing than at hand washing.
- If we simplify the model and do not incorporate the knowledge of numbers of table-companions from the third Dutch National Food Consumption Surveillance as discussed in section 3.2.7., assuming people ingest all campylobacter transferred to salad by one fillet, the relative risk increases to 180%.

4.3.6 Dose-response

- If $P_{ill|inf} = 0.33$ is modified to 25% and 40%, this modifies the relative risk to 78% and 122%, a linear effect.
- When, for the new dose-response model, the hazard function derived by Teunis et al. (2005) was used as a description of the probability of illness given infection, instead of the fixed probability $P_{ill|inf} = 0.33$, this gives an increase in the relative risk for this model to 160%. (This result could not be shown in fig 4.17.)

5. Discussion

5.1 Chicken meat as a source of campylobacteriosis

In Chapter 2 the sources of human exposure to Campylobacter are studied by two different approaches: a laboratory driven case-control study and an exposure assessment. Both approaches show that chicken meat is an important transmission route, but not the only one. In the exposure assessment direct contact to animals (cats and dogs at home, animals at city farms and at farms in general) and food are identified as the major categories of exposure. The case-control study points at (unintentionally) undercooked meat as another relevant source and the (deliberate) consumption of raw meat is identified as important in the exposure assessment. However, routes other than cooked chicken meat are not included in the risk model described in the other chapters of this report. This choice has been made at the start of the CARMA project, based on discussion with the risk management and the need to restrict the risk model to allow a complete quantitative analysis. Clearly, the other routes should be a focus of campylobacter risk assessment in the future.
Of the other transmission routes of campylobacter, exposure due to undercooked chicken meat may quite easily be incorporated in the model presented here. The industrial processing model is directly applicable, but the chicken meat product may be different and the consumer phase model should include the effect of undercooking. Basically, these new components of the model will predict that only a fraction of campylobacters on the carcass after processing will survive and will ultimately be ingested by the consumer. When implemented in models, this has a similar effect as cross-contamination, which also results in a fraction of the campylobacters being ingested. So, although the exposure distribution may be modified, there is no reason to expect that the effects of interventions in the production chain before the consumer phase will be very different when undercooked meat is incorporated in the analysis.
The percentage of human cases of campylobacteriosis that are the consequence of chicken meat preparation and consumption is not evident yet. In the case-control study the population attributable risk (PAR) of chicken consumption is found to be 23% of indigenous cases or 19% of all cases (including those which are travel-related), in the exposure assessment it is among the more important routes. Another interesting observation is that of Vellinga and Van Loock (2002) during the dioxin crisis in Belgium in 1999, which led to a ban on chicken meat and eggs for four weeks. Here the incidence of campylobacteriosis dropped by 40%, indicating that this is the relative contribution of chicken meat to the incidence of campylobacteriosis in this country at the Dutch border. This percentage is considered to be the upper limit for the Netherlands. Hence, our best estimate of the contribution of chicken meat to the Dutch incidence of campylobacteriosis is 20% with an upper limit of 40%.

5.2 Baseline

The baseline risk model is a representation of the most likely situation for broiler chicken meat produced in the Netherlands in 2000, from birds reared in Dutch farms, calculating the risk for Dutch consumers. It uses most likely values for the model parameters, including variability in levels of campylobacter between flocks and between birds (and carcasses) within a flock, stochasticity in faecal leakage, variability in effects of storage between industrial processing and consumer food preparation, and variability in food preparation and consumption.

The results show that, on average, there is a continuous decrease in the level of Campylobacter on the carcasses and the meat, N_{ext}. This is the consequence of the absence of growth and the repeated inactivation and removal of Campylobacter during processing, as a consequence of submersion, washing, defeathering, skinning, storage etc. Contamination of the carcass exterior by faeces leaking from the carcass (predominantly during defeathering) may give a temporal increase in the level of Campylobacter when the concentration in the faeces, C_{fec}, is relatively high and N_{ext} is relatively low (see fig 4.9). On average this effect is dominated by a continuous decrease because (1) with a lower animal prevalence for many birds $C_{fec} = 0$, whereas it is assumed that N_{ext} is always > 0 and (2) apparently values of N_{ext} are relatively large compared to values of C_{fec}. The reason for both (1) and (2) is that apparently the bird's exterior is already heavily contaminated with faeces at the entrance of the processing plant. Furthermore, results show that cross-contamination during processing and food handling leads to a dispersal of campylobacters over the units (birds, carcasses, fillets) involved, and as a consequence the prevalence of contaminated units may increase, whereas the variability between units decreases (see also Nauta et al. (2005)).

An interesting finding is that, although on most carcasses the bird's exterior is the source of the majority of campylobacters on the chicken breast ($N_{ext, f}$), those originating from the leaking faeces cause about 70% of the cases of human campylobacteriosis (see fig 4.18). This is a consequence of the variability due to the large standard deviation of the lognormal distribution describing the input values of the concentration of Campylobacter in the faeces, C_{fec}. This implies that, sometimes, very high numbers of faecal bacteria are transmitted to the carcasses. These peak numbers drive consumer risk to a large extent.

The uncertainty about the baseline risk estimate is large, and is only analyzed quantitatively to a limited extent. Reasons for this are that at some stages it is very hard to quantify uncertainty, that it was difficult to implement the uncertainty in the risk model, and that the final interpretation of this uncertainty is complex. However, uncertainty in parameter estimates was incorporated in the expert study performed for the processing model (Van der Fels-Klerx et al. 2005). Analyses of these results show that the uncertainty is large (see section 4.3.3). Furthermore, uncertainty is explored in the analysis of alternative scenarios, as discussed below in section 5.4. Its impact on the relative risk is discussed in section 5.5.3.

The ingested doses at exposure are generally very low, the majority only one or two cfu. This corresponds to for example a previous risk assessment result concerning Shigatoxin producing *E. coli* O157 in steak tartare (Nauta et al. 2001). It is the consequence of the fact

that the distribution describing the variability of numbers of pathogens in and on food units is shifted to lower values by processing. When the distribution shifts to the left, only the right hand trail remains (the rest of the distribution shifts to a value of zero), and the majority of numbers remaining is very low. For a risk estimate this is rather troublesome, because dose-response information usually concerns much higher doses, and the estimated effects of low doses have to be assessed by extrapolation. The classic dose-response model applied here predicts 1.9% probability of infection and 0.6% probability of illness when 1 cfu campylobacter is ingested, and the new model predicts even 68.6% probability of infection and 22.6% probability of illness when 1 cfu is ingested. These estimates deviate substantially and are crucial for the final prediction of the number of cases, but also quite uncertain. They are based on inference of results of higher or unknown (for the new model, see Teunis et al. (2005)) doses, in a food matrix different from chicken meat and salad. Nonetheless, it is the best we can get at the moment.
The baseline estimate of 12327 cases of campylobacteriosis as a consequence of the consumption of salad cross-contaminated after handling chicken breast fillet, should be interpreted with regard to the identified uncertainties. Throughout the analysis the relative impact of interventions and alternative scenarios, expressed as relative risk, is the preferred output measure.

5.3 Interventions

The predicted effects of a list of interventions are shown in section 4.2. These interventions aim at different stages of the production chain and at the consumer. Here we regard the assessed effect on the relative risks of these interventions only. Costs and social acceptance are analyzed together with these assessments elsewhere (Mangen et al. 2005a, Bogaardt 2005).
The risk model analysis shows that the most effective intervention at the farm may be improvement of hygiene. However, the precise measures that are needed at the farm to achieve the desired effect could not be identified. As a consequence, the predicted effect of this intervention is quite uncertain. It seems that hygiene at the farm alone will not be sufficient to eradicate Campylobacter from the broiler chicken meat production chain. This intervention is discussed further by Katsma et al. (2005). Phage therapy, an intervention at the farm shortly before slaughter, is predicted to be quite effective. It is an intervention which is still under development and its effectivity in practice should probably be tested more extensively. Alternatively, the use of bacteriocins may be a method which can achieve similar results (Svetoch et al. 2003) .
In this report, scheduled treatment refers to a separate treatment of positively and negatively tested flocks, without necessarily changing the order of processing. Negative flocks get no extra treatment, whereas positive flocks do. The farm model (Katsma et al. 2005) predicts that about 20% of the contaminated flocks have a low animal prevalence (<5%), which will easily remain undetected if flocks are tested for Campylobacter at the farm. The inevitable

presence of false negative flocks makes it very difficult for scheduled treatment to guarantee a special treatment of all contaminated flocks.
It was found earlier in the CARMA project that logistic slaughter, a special form of scheduled treatment where positive flocks are processed at the end of the day to prevent cross-contamination to negative flocks at the processing plant, is expected to be not very effective (Evers 2004, Havelaar et al. 2004). False negative flocks will have a significant effect on lowering the effect of this intervention and the average level of contamination of carcasses from cross-contaminated flocks will be several log units lower than the average level of positive flocks. Furthermore, it is difficult to implement this intervention by the processing industry, especially in combination with logistic slaughter for Salmonella. Scheduled treatment only is easier, because here only the treatment of the flock is different, depending on the status of the flock. The order of processing of the flocks on the day of slaughter need not be modified with scheduled treatment.
We compared three different test methods, the classic culture test, and two newly developed tests, PCR and dipstick (see also Katsma et al. (2005)). These tests differ in sensitivity and specificity, and in the required time span between sampling and test result. The most effective test will combine a quick and easy test (like the dipstick) with a high test sensitivity (like PCR). Results show that PCR seems to be the most efficient testing method. However, this method is still under development.
Intervention is most effective during processing. In this stage intervention can aim at the campylobacters in the gut (C_{fec} and thus N_{fec}) and at campylobacters on the exterior (N_{ext}). Phage therapy (which is actually administered at the farm) and reducing faecal leakage are directed at the former, decontamination (by chemicals, cold, heat or irradiation) is directed at the latter. Lowering the contamination at the exterior is most effective after evisceration, when cross-contamination (or recontamination) by faeces is no longer possible. Of the methods that aim to do so, irradiation is most effective, but its suitability for implementation is disputable (Mangen et al. 2005a, Bogaardt 2005). Decontamination by lactate or TSP before chilling seems to be a simple and relatively effective intervention.
As a combined intervention aiming at the reduction of both N_{fec} and N_{ext} seems very promising, an additional model run was performed in which interventions VI and VIIILb were combined. If faecal leakage is decreased (reduction of C_{fec} by 6 logs) and the carcass is decontaminated with lactate before chilling (reduction of $N_{ext, wash}$ by 1.3 logs, the risk reduction is 98.3%, so the relative risk is 1.7%. The mean value for log $N_{ext, cutting}$ gets down to 0.57. This result confirms that a combined approach, aiming at both campylobacters in and on the carcass can be very successful.
Intervention at the consumer stage is considered by performing a mass media information campaign. The effectivity of such a campaign is hard to predict, but will probably be limited. A recent Dutch study shows that consumer food preparation behaviour is largely habitual, and therefore difficult to change by just launching an information campaign (Fischer et al. 2005). In the risk model, the effectivity of intervening in the consumer phase is predicted to be very small.
For the whole chian, it can be concluded that intervention at the processing plant is most promising, certainly when intervention aims at both reduction of faecal contamination and/or

faecal leakage during processing, and decontamination of the carcass exterior. Hygiene at the farm is important to minimize the input of campylobacters into the system. Scheduled treatment may be a good option if differentiation in chicken meat products (e.g. fresh and processed) is acceptable. However, it seems that none of these interventions can guarantee the sales of campylobacter free chicken meat. This will only be achieved by irradiation.
As the baseline model predictions are uncertain, the predicted effects of interventions are uncertain too. Moreover, the effects of many of the interventions were difficult to quantify. If measured, the quantitative effects of some frequently proposed decontamination methods (like the use of lactate and TSP) are poorly documented in the literature. As discussed further below (section 5.5) it is very difficult to quantify the total uncertainty as it is a combination of uncertainty based on assumptions (e.g. on representativity), simplifications and statistical uncertainty. The quantitative predictions should therefore be treated with quite some reservation. However, the qualitative conclusions drawn in this section appear to be quite robust. Intervening by lowering the levels of both campylobacters in and on the carcass will be effective regardless of many of the model assumptions.

5.4 Alternative scenarios

Alternative scenarios are explored to test the impact of model assumptions, input values and parameter estimates. This gives insight in the robustness of model results and important gaps in knowledge.
Input distributions of $N_{ext,input}$ and C_{fec} are based on a limited data set. The variability between flocks and between birds appears to be large, and the description of these variabilities has considerable impact on the final results of the model. In the model we assume for simplicity that N_{ext} and C_{fec} are not correlated, an assumption which appears to have little impact on the end result. The assumption that, even if the prevalence of infected animals is low, all birds of infected flocks are contaminated on their exterior at the entrance of processing presumably has little impact, as lowering the mean value of N_{ext} has less effect than changing C_{fec}. A decrease in C_{fec} by one or two log levels has only little less effect than lowering it by higher levels. This suggests there is some threshold concentration in the faeces, below which the campylobacters in the chicken faeces are irrelevant for the final contamination of the meat. This finding is also important in the light of intervening by reducing faecal leakage or phage therapy. Reduction by a few log levels may be almost as effective as elimination of campylobacter from the faeces.
The effect of incorporating variability in levels of campylobacter both between and within flocks is very large. The reason for this finding is the assumed lognormal distribution of concentrations and numbers of campylobacter. Numbers of microorganisms are usually expressed in logs. It is however important to realize that the mean of the logs, the geometric mean, is lower than the arithmetic mean (If you take $10^{Normal(\mu,\sigma)}$, the ^{10}log of the arithmetic mean of the number of Campylobacters is $\mu + \sigma^2 \ln(10)/2$). The arithmetic mean is the value which best represents the total amount of campylobacters in the processing chain. In the dose-response relationship the effect of these campylobacters is not logarithmic, but

approximately linear for low doses, which are dominant in this risk assessment. As a consequence, omitting the variability in the analysis by putting $\sigma = 0$, lowers the exposure dramatically, and thus also the predicted number of cases.
Further analysis of the industrial processing model and the uncertainty identified in the expert study shows that the uncertainty about the model parameters for the defeathering stage has the most profound effect on the total uncertainty. This implies that more quantitative data on the effects of processing at the defeathering stage can effectively lower the total uncertainty of the model predictions. The bimodal uncertainty distribution of the model parameter $b_{env,def}$ is interesting and even affects the shape of the uncertainty distribution of the level after cutting. The bimodality is a consequence of the analysis (see also Cooke et al. (2004)) and may reflect that experts are in two minds about the true value of this parameter.
It appears that the choice for weighing the experts as we did (using the optimized decision maker as described by Van der Fels-Klerx et al. (2005)) has relatively little impact on the predicted number of cases. However, the uncertainty about the effects of processing may be quite different between the three weighting schemes applied, as the uncertainty distributions of the model parameters resulting from the expert judgement study may differ substantially. When experts are not weighted, the total uncertainty increases substantially (data not shown).
The model for the stages cutting and storage are based upon a very limited amount of data, on the opinion of only one consulted expert and some additional guesses. The alternative scenario analysis shows that taking different (but feasible) values for π (referring to the amount of campylobacter transmitted from carcass to fillet) and $r_{storage}$ may have considerable impact on the end result. Therefore, more and better quantitative data on these processes may substantially lower the final uncertainty of the model predictions too.
The data used for the consumer phase model are generally not specific for Campylobacter and the preparation of a salad along with chicken breast fillet. They are, however, the best quantitative data we could find in the literature. The frequencies of handling are based upon statements of consumers, which may not reflect their actual behaviour (Redmond and Griffith 2003). Therefore, the uncertainty about these parameters is quite large too. Quantitative observational data on human behaviour should be gathered to get better information on these food handling frequencies. The analysis of alternative scenarios shows that the effect of individual parameter estimates is not very large if compared to other risk model parameters.
The impact of the uncertainties in the dose-response model as investigated in our analysis is not very large either. However, the new model predicts about 14 times more cases of campylobacteriosis, due to the much larger probability of illness due to low doses as explained in section 4.1. This implies that the choice of the hazard model or fixed probability of illness given infection is less important than the choice for a model for the probability of infection. The difference between the shapes of the potential dose-response curves for campylobacter as illustrated in fig. 3.5 is remarkable, and shows that the dose-response relation for campylobacter is still largely unknown and needs more research.

5.5 Uncertainties

Addressing and quantifying uncertainties is an essential part of risk assessment. Unfortunately, we have not been able to fully implement this quantification here, so it is difficult to make explicit statements about the uncertainty of our conclusions.
To clarify the context of the model described in this report, the ten key simplifying assumptions made are listed in the Box I. These assumptions had to be made to allow doing a quantitative risk assessment which evaluates the effects of interventions in the food chain on an exposure distribution to Campylobacter. The validity of these assumptions may be a topic of further discussion, and their consequences for risk assessment and the results presented in this report may be the subject of further research.
Some of the assumptions mentioned need some special explanation, and are discussed below.

5.5.1 Expert judgement as data source

The expert judgement study performed for the CARMA project (Van der Fels-Klerx et al. 2005) is an essential part of the risk model and the methodology applied. This structured expert study was done after the processing model was constructed, in line with the MPRM methodology, which puts the model construction step before data collection (Nauta 2001, Nauta 2002). From this expert study, we obtained estimates of the processing model parameters which we could not have obtained otherwise. As the processing model includes the combined cross-contamination and inactivation/removal dynamics and differentiates between campylobacters on the exterior and in the faeces leaking during processing, it is expected to better reflect the transmission of Campylobacter during chicken processing. Therefore it is expected to better predict the effects of interventions than a linear model based on a set of count data obtained along the processing lines (e.g. Oosterom et al. (1983), Berrang and Dickens (2000)). Also, the expert data better reflect the situation in the Netherlands in the base year 2000 than any other data available.
Of course, there is a disadvantage in applying expert judgement instead of microbiological data, as expert judgement inevitably includes the subjectivity of the consulted experts. Experts may be biased and wrong. To deal with this fact as best as one can, the experts have been calibrated and weighted in the expert judgement study. The effect of the weighing scheme applied has been evaluated in the list of alternative scenarios (section 5.4) and shows to have some impact, but not very much. This could be studied further in the future.
The alternative, applying microbiological data, has some drawbacks too. First, such data may not be representative for the Netherlands in the base year 2000, and are not directly applicable in the processing model. Also, like expert judgement data, microbiological data may be biased as a consequence of the microbiological techniques that are applied when counting campylobacters on poultry carcasses. (The procedure applied to wash-off the campylobacters from the carcass, for example, is not perfect, because it is extremely difficult (if possible at all) to wash off and count everything that is on a carcass.) Also, microbiological data usually lack important information of the history of the processed flocks. Ideally, the same flocks are sampled and campylobacters counted at a series of stages

BOX I. Ten key simplifying assumptions of the risk assessment

1. **Process model**: The process modelled is representative for broiler chicken processing in the Netherlands in the base year 2000.

It is not possible to include all variations in processing that exist nationwide. Stakeholders have agreed that the processes of producing broiler chicken meat are sufficiently similar to allow the use of one process model.

2. **Models**: The (cross-contamination, survival, removal) models applied for the modules in the risk model are suitable to quantitatively describe the transmission dynamics of Campylobacter along the chain of production and consumption of broiler chicken meat.

This is common practice in Quantitative Microbiological Risk Assessment.

3. **Data**: The data applied are representative for broiler chicken processing in the Netherlands in the base year 2000; counts properly reflect the numbers of viable campylobacters on the counted objects.

Scarcity of quantitative data does not permit an alternative. The model shows that good quantitative data are crucial for a good evaluation of interventions during processing. Collection of quantitative data, in particular on variability in numbers and concentrations, is indicated as a future research priority.

4. **Expert judgement**: The parameter value estimates based on expert judgement, obtained by a structured expert judgement study or otherwise, are a correct reflection of transmission dynamics of campylobacters in the Dutch broiler processing chain in the base year 2000, and are as representative as the other data applied in the model.

A structured expert judgement study was performed to obtain representative quantitative data for the processing model parameters. The mechanistics included in this newly developed model are essential for calculation of the effects of interventions during processing. As it was not possible to apply a structured expert judgement study for all unknown parameters, less formal procedures had to be used to complete the risk model. Especially the effects of deboning, cutting and storage need further study.

5. **Campylobacter**: All thermophilic campylobacters on broiler chickens and meat can be treated alike; there are no differences in attachment properties, viability, virulence etc.

Variation in these characteristics between Campylobacter strains may be quite important, but information that can be incorporated in the risk assessment is lacking. To date, typing studies indicate that it is not (yet) possible to differentiate between virulent and less virulent strains of Campylobacter (Wassenaar et al. 2004).

6. **Dose-response**: The dose-response relationship can be applied for all campylobacters to which the Dutch population is exposed.

The 'classic' dose-response model is based on a study with young healthy male volunteers, the 'new' model incorporates data on two outbreaks among school children drinking raw milk. The first is generally applied in Campylobacter risk assessment and was also our choice for the baseline model.

7. **Interventions**: The quantitative effects of each of the interventions on the model parameters are properly assessed.

These estimates are based an the available quantitative data. Alternatives are explored in the uncertainty analysis of the effects of interventions (error bars in fig 4.13)

8. **Extrapolation**: Consumption of salad cross-contaminated by chicken breast fillet is representative for all human exposure to campylobacter via chicken meat

It is not possible to model all possible exposure pathways in detail. This specific pathway is generally considered important both in frequency of occurrence and potential risk, and includes all relevant food preparation processes that may lead to exposure, except undercooking.

9. Cooking: Campylobacters do not survive cooking of chicken meat.

Low temperatures at 'protected areas' in the meat or insufficient heating of chicken meat during cooking may lead to survival of Campylobacter (Anonymous 2001, Anderson et al. 2003). This is not incorporated in the risk model because it is thought to be a minor source of exposure. As indicated in section 5.1 it is not expected that this assumption will have a major effect on the relative risk associated with interventions preceding the consumer phase.

10. **Relative Risk**: the predicted relative risk and risk reduction, used to predict the effect of interventions on the public health burden, are not very sensitive to the assumptions made and uncertainties attending the risk estimates.

Due to the complexity of the model and the need to incorporate within- and between-flock variability, we have not been able to perform a full quantitative analysis on this issue. It is reasonable to expect that the uncertainty in relative risks (which are a quotient of risks) is far less than the uncertainty in absolute risk estimates. The impact of this assumption should be a future research priority in the development of risk assessment methodology. (See also section 5.5.3.)

from farm until the end of processing. Hence, being the result of another imperfect tool, we decided to use the available microbiological count data for validation in this study, as discussed in section 5.6.1.

5.5.2 Extrapolation

The results of the risk model relating to the effects of intervention are extrapolated from the modelled chicken meat meals with cross-contaminated salad after cutting fillet, to all consumed chicken products. Hence the results of a fine and precise analysis are assumed to be representative for all sorts of meals prepared with chicken meat: whole grilled chickens, barbecues with chicken meat, fried legs etc. As we only consider cross-contamination in our risk model, risks associated with undercooking are not incorporated in the model.
The pragmatic approach of this risk assessment has been that it is better to make a precise model for one product than a less precise model for all. This allowed us to include non-linear dynamics related to cross-contamination, presumably the process leading to the highest exposure. By choosing a meat product frequently eaten in the Netherlands, and a route of (cross) contamination considered important by many, we aimed to get important insight in the dynamics leading to exposure to campylobacter via chicken meat. Further research could focus on the preparation and consumption of chicken meat with skin (where higher level of campylobacter may be expected on the raw meat) and for example barbecue meals where cross-contamination and undercooking may be more frequent. As indicated in section 5.1, it may be expected that the effects of undercooking are not basically different from those of cross-contamination in the domestic environment, so that the effects of interventions in other parts of the food chain are probably similar. However, this should be confirmed by future research.

5.5.3 Relative Risk

The estimated relative risks are the most important results of the risk assessment, as they are the primary base of the response to the questions posed by the risk management. Therefore it is important to reflect on the uncertainty about these relative risks.
Due to the complexity of the model and the need to incorporate within- and between-flock variability, we have not been able to perform a full quantitative analysis on the uncertainty in the relative risks. It is reasonable to expect that the uncertainty in relative risks (which are a quotient of risks) is less than the uncertainty in absolute risk estimates: the uncertainty in the numerator and the denominator may (partly) cancel out if both are larger or smaller than stated in the baseline. This yields a good argument to believe that, in general, the predicted (ranking of) relative risks is rather insensitive to the uncertainty in the model parameters.
In this context, the philosophical interpretation of the uncertainty that can be quantified if research time and resources allow this, is important. Uncertainty that represents 'how certain we are that a statement is true', is usually a belief, and depends on assumptions made by the researchers and stakeholders. If the uncertainty about all parameters is quantified, this is always based on some prior beliefs and (simplifying) assumptions, and therefore this quantified uncertainty is dependent on a set of assumptions: the uncertainty itself is uncertain

too. Hence, even if performed, a full quantitative uncertainty analysis may suggest there is a 'true' uncertainty, and by that mislead the risk managers.
In the model presented here, there is uncertainty as a consequence of the simplifying assumptions (see Box 1), uncertainty in the (representativity of) data, statistical uncertainty, etc. The effects of some of these sources of uncertainty can be explored. The uncertainty in the effects of interventions, for example, are analyzed and results are given by the error bars in fig 4.13. (But note that this uncertainty depends on some assumptions too.) Also, the uncertainty in the parameter values estimated by the expert judgement study, is fully characterized (see the Appendix).
Although, for reasons of complexity as indicated above, we have not been able to quantify the uncertainty about the processing model in our analysis, some extra model simulations were run to explore the effect of uncertainty in the input values and the effect of the quantified uncertainty in processing model parameters on the relative risks of some interventions. The results of these exploratory analyses are given in table 5.1 and fig 5.1.
First, the effect of uncertainty in $C_{fec\,\mu}$ on the predicted relative risks of some interventions is studied. Taking log $C_{fec\,\mu} = 4$, that is a decrease by two logs, has considerable impact on the relative risk of interventions aiming at this particular parameter (see table 5.1). Given the alternative scenario results shown in fig 4.17 this is not unexpected. The maximum effect of lowering C_{fec} inevitably decreases if the initial value of C_{fec} is lower. Hence, although a 2 log reduction in $C_{fec\,\mu}$ is rather large, this example shows that uncertainty in this input variable can have quite some effect on the estimated relative risk of the interventions 'phage therapy' and 'reduction of faecal leakage'.

Table 5.1 Relative risks of some interventions given that the mean concentration in the faeces $C_{fec\,\mu}$ is 2 logs lowers than assumed in the baseline.
Baseline results are compared with this alternative. The effects of interventions aimed at reducing carcass contamination by campylobacters in the faeces decrease strongly, effects on two other interventions are small.

	baseline	$C_{fec\,\mu}$ - 2 logs
phage therapy	25.6%	89.2%
faecal leakage	22.9%	89.2%
1x decont. lactate	12.1%	8.1%
farm hygiene	57.1%	55.8%

Next, the uncertainty about the processing model parameters is taken into account by taking ten random sets of samples from the (interdependent) uncertainty distributions of these parameters, derived from the expert study (see Appendix). When the relative risk of intervention VIIILb, submersion of carcasses in lactate between washing and chilling, is calculated for each of these ten sample sets, it varies between 10.1 and 23.7%. So the uncertainty range of the risk reduction is at least between 76% and 90%, where the estimate based on median processing model parameter estimates is 87.9% (see table 4.3). As illustrated in fig 5.1, large relative risks are associated with high estimates of the incidence of campylobacteriosis. The uncertainty in the relative risk is much lower than the uncertainty in

the incidences with and without interventions. The uncertainty is partly cancelled out in the calculation of the relative risk, but not completely.

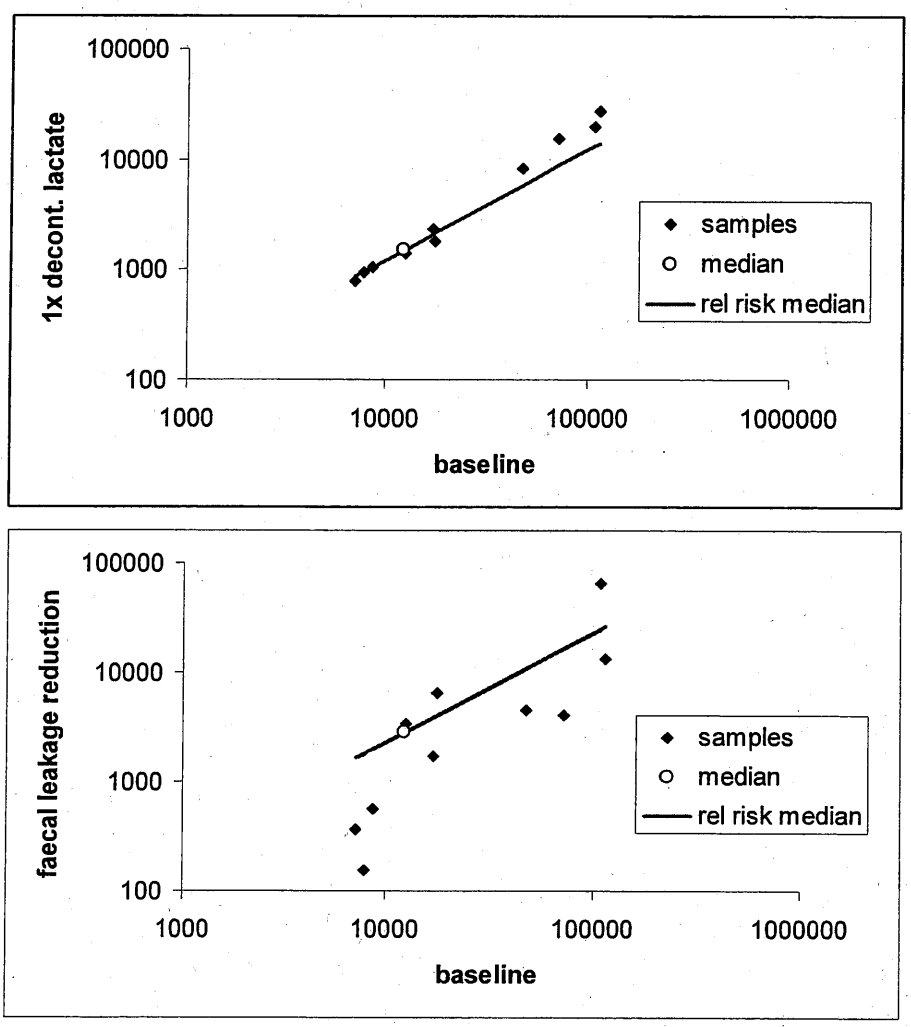

Figure 5.1 Incidences (cases per year) predicted by the baseline model plotted against incidences predicted after intervention.
The circle indicates the reported result (table 4.3), taking median values for the processing model parameters. Other dots show the result for ten random samples from the uncertainty distributions obtained from the expert study. The line maps relative risks equal to that of the median result.
Above: results for the intervention 'submersion of carcasses in lactate between washing and chilling', with relative risk of 'median' 12.1%. For higher incidences relative risks are larger (and risk reductions are smaller), but the uncertainty in relative risks is much smaller than the uncertainty in incidences.
Below: results for the intervention 'reduction of faecal leakage', with relative risk of 'median' 22.9%. For this intervention the uncertainty in relative risks is much larger.

However, when the relative risk of intervention VI, reduction of faecal leakage, is calculated, the uncertainty appears to be very large. Here the uncertainty range of the risk reduction is at least between 41% and 98%, where the estimate based on median processing model parameter estimates is 77.1% (see table 4.3). As shown in fig 5.1, the correlation between baseline incidence and predicted incidence after intervention is much lower than for the other

intervention. Apparently the uncertainty of the expert panel about the processing model parameters has considerable impact on the uncertainty of the risk reduction due to 'reduction of faecal leakage'. The probable reason for this is that this intervention is aimed at the start of processing, so that uncertain parameters at several processing stages will have more influence on this intervention than on an intervention at the end of processing.
Summarizing, it is shown that the estimated relative risks are less uncertain than the incidence, but may still be substantially large. The examples of uncertainty analysis clearly illustrate that it is worthwhile to extend this uncertainty analysis by additional research.

5.6 Model Validation

Some data are available that can be used for validation of the model. It should be noted beforehand that the impact of this validation on the validity of the effects of the interventions, the most important aspect of this risk assessment, is not evident. If model predictions of the baseline study on the situation in 2000 appear correct, this does not mean that the relative risks associated with the interventions are properly predicted, because the effect of these interventions on the model parameters may be improperly assessed due to a lack of data. Also, if predicted values are not validated, this does not imply that the predicted effects are wrong because the (ranking of the) relative risks may be assessed quite well. Nonetheless, good correspondence between the model and data from the real world will of course be regarded as a good support for the model and the risk assessment.

5.6.1 Processing model

In the summer of 2004 we sampled a set of flocks for numbers of Campylobacter at different stages of processing (Jacobs-Reitsma et al. in prep.). For two of these flocks we sampled carcasses and fillets at the relevant stages, for a third flock all but the caecal content data yielded quantitative data. First, the number of campylobacters per sample is estimated by MLE fitting to a Poisson distribution of counts per sample, using all count data (including data of upper and lower limits, if the dilution series applied appeared to be inefficiently chosen to obtain proper counts). Next, the results for the different samples within a flock (expressed in logs) are fitted to the best fitting normal distribution, also using MLE, to obtain a distribution describing the variability between units.
Results as shown in table 5.2 and fig 5.2 are caecum counts per gram for two flocks, exterior before processing (carcass with feathers; cfu per carcass), carcass after chilling, chicken breast fillet after cutting, and chicken breast fillet after cool storage at 4°C for one week.
For validation, the processing model was run with the count data for C_{fec} and $N_{ext,\ input}$ as input values, for flocks 1 and 3, assuming 100% animal prevalence, incorporating the uncertainty in the parameter estimates of the processing model. Results (see fig 5.3) show that for flock 1 the model prediction for the level of contamination after chilling is too high, but it is within the 90% uncertainty range for flock 3.

Table 5.2 Results of fitting count data of three flocks processed in The Netherlands in 2004 (Jacobs-Reitsma et al. in prep.).
Mean and sd are the mean and standard deviation of the normal distribution fitted through the log counts.

		flock 1		flock 2		flock 3	
		mean	sd	mean	sd	mean	sd
caecum	C_{fec}	9.2	0.46	> 5		7.77	0.4
carcass with feathers	$N_{ext,\ input}$	8.03	0.5	7.39	0.5	6.39	0.69
carcass after chilling	$N_{ext,\ chill}$	5.16	0.56	5.26	0.32	5.18	0.24
fillet after cutting	$N_{ext,\ f}$	3.53	0.29	4.01	0.48	2.96	0.26
fillet after storage	$N_{ext,\ fs}$	3.42	0.39	2.75	0.44	2.19	0.31

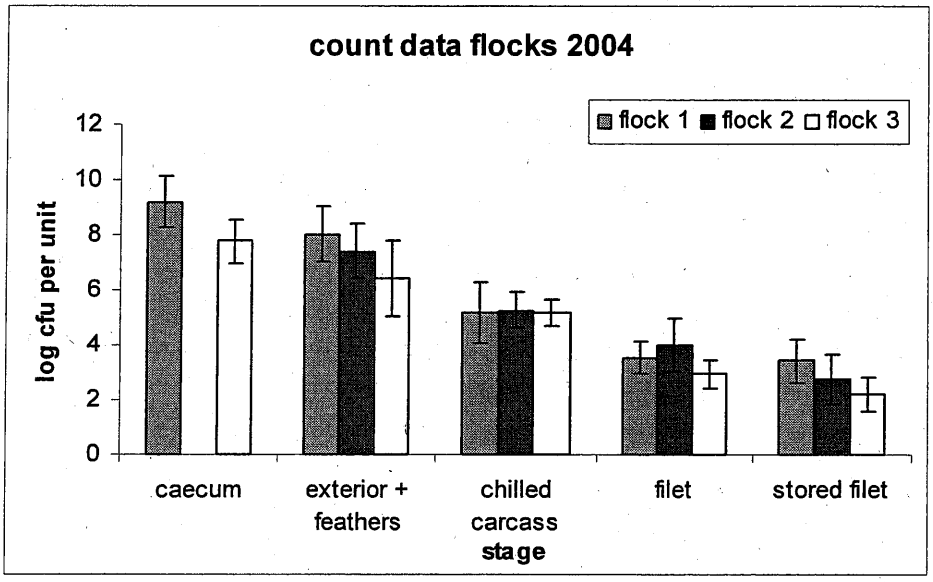

Figure 5.2 Overview of count data of three flocks processed in the summer of 2004 in the Netherlands (Jacobs-Reitsma et al. in prep.).
Error bars indicate 95% interval (= 2*sd) of variability in counts between carcasses/fillets from the flock.

The mean level predicted for flock 1 carcasses after chilling is 7.24 (sd 0.24) and on the fillet 4.59 (sd 0.07), much higher than means of the count data 5.16 and 3.53 (table 5.2). The mean level predicted for flock 3 carcasses after chilling is 5.77 (sd 0.23) and on the fillet 3.09 (sd 0.07), close to the means of the count data 5.18 and 2.96. The decrease in standard deviation as predicted by the model can be found in the data, be it to a smaller extent. This higher standard deviation in the data may be explained by the uncertainty associated with the counting method.
This comparison of model predictions with independent count data does not allow a clear statement about validation. For one flock the model predictions and count data fit quite well, for the other they do not. Note that in flock 1 C_{fec} has very high values, based on counts of caecal contents. As mentioned in section 3.3.2 the campylobacter concentration in the caecum is usually higher than that in the leaking faeces. Hence, the count data may not be

representative for C_{fec} as applied in the model and overestimate the concentration in the leaking faeces. If, for example, the model is run for flock 1 with the probably more realistic mean of C_{fec} 1.5 log lower (7.7), the 90% CI for the level after chilling is 4.8 - 7.2 log cfu per carcass, and includes the data mean 5.16.

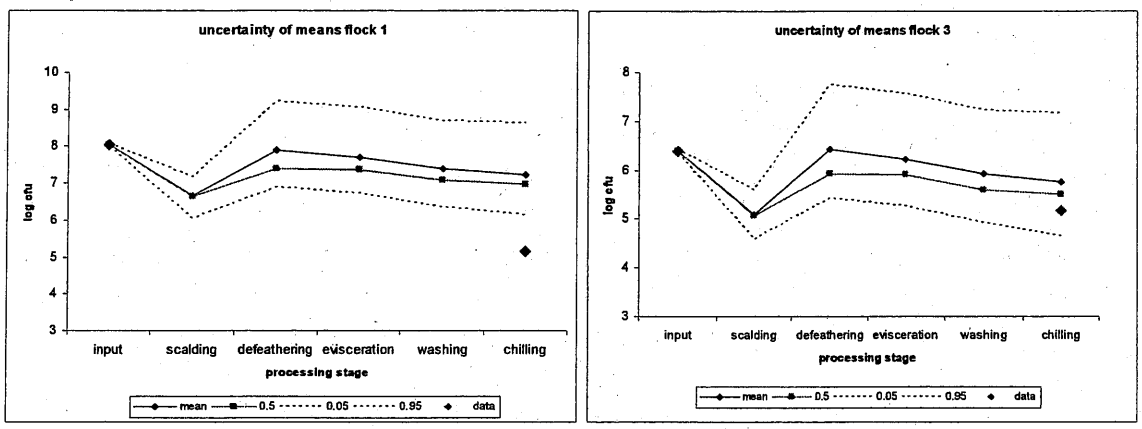

Figure 5.3 Results of validation runs of the model, using count data of carcasses processed in the Netherlands in the summer of 2004.
The lines are model predictions for log (N_{ext}), the red dots are data points measured by Jacobs-Reitsma et al. (in prep.). The predicted increase in log (N_{ext}) after defeathering is a consequence of the relatively high values of C_{fec}.

In her risk assessment study on Campylobacter in chicken, Hartnett (Hartnett 2001, Hartnett et al. 2002) uses count data of several studies on Campylobacter during chicken processing. These count data (Oosterom et al. 1983, Izat et al. 1988, Berrang and Dickens 2000), report a decrease of 0.7 to 3.4 log units decrease due to soft scalding, an increase (up to 2.8 log units) or decrease (up to 0.8 log units) by evisceration, and again a substantial decrease due to washing (0.4 to more than 3 log units). For defeathering she has developed a cross-contamination model and does not apply the data of Oosterom et al. (1983), showing a change in level of campylobacter on the pericloacal skin between -0.2 and 1.6 log units (i.e. on average an increase in number of campylobacter). So international data point at occasional increase in level during defeathering and evisceration and a relatively strong decrease during washing. This is different from the results presented for our baseline model, where the numbers of campylobacter on the exterior (slightly) decrease over the processing stages.
It is not evident how the reported data can be used for model validation. Not only may the processing practices be different from the common situation in the Netherlands in 2000, also the application of means of restricted data sets of different birds from the same flock for validation of a model on changes in levels on individual birds is complex. (See Nauta et al. (2005) for discussion on this issue). The increase in level during defeathering fits in the model used in this risk assessment: as illustrated in figs 4.9 and 5.3, when C_{fec} is relatively high compared to N_{ext} this may give an increase in level after defeathering and, occasionally, during evisceration. Apparently, in those processing lines where an increase in levels of contamination was found, the leaking faeces is an important source of Campylobacter

contamination of carcasses. Overall, the variability in data fits well with the variability in the model results of the risk model

5.6.2 Monitoring results

The Dutch Food Inspectorate monitors chicken meat on the presence of Salmonella and Campylobacter. In 2000, 30.5% of the chicken meat products at retail was found to be contaminated with Campylobacter (Van der Zee et al. 2002). This value is an intermediate value compared to results in surrounding years. It is less than the percentage of products expected to be contaminated in our model. Although this percentage is not explicitly modelled, we assume a flock prevalence of 44.4% and find 94% of the fillets from contaminated flocks contaminated after cutting, yielding 41.7% contaminated overall. However, the percentage assessed by the model is expected to be larger than the percentage found in monitoring, because with the current detection methods low numbers of Campylobacter may not be detected. A closer look at the results of the baseline model shows that 30.5% of the fillets after cutting would be expected to be positive for Campylobacter if the detection limit of the method applied in the monitoring program is 20 cfu. This 20 cfu seems to be a reasonable value for such a detection limit, so it can be concluded that our model results are in line with the monitoring results.

5.6.3 Fillet counts

As shown in table 3.4 in section 3.2.4., in the summer of 2004 we counted campylobacters on fillets directly after cutting and after storage at 4 °C (Jacobs-Reitsma et al. in prep.). Within flocks means of logs in six sampled flocks are between 2.9 and 4.0 log cfu, with mean 3.3. These values are considerably larger than the predicted mean (1.97 log cfu for fillet after cutting), and lie at the upper end of the distribution of means per flocks as predicted by the model (50% 2 log cfu, 95% 3.9 log cfu). The correspondence between the data and the model improves somewhat if it is taken into account that the count data are from chicken products of flocks tested positively at the farm. If we consider these flocks only, the median mean level on the fillets is 2.3 log cfu and the 95%-ile is 4.1. Still, this comparison suggests that the model underestimates the level on the fillets after cutting, which, like the alternative scenario analysis, supports the need for more research on the effects of cutting on campylobacter contamination. Note however that, if this finding is correct, an underestimation by the risk model of the level of contamination coincides with an overestimation of the predicted number of human cases of campylobacteriosis. This is a similar result as in a previous risk assessment of STEC in steak tartare (Nauta et al. 2001).

5.6.4 Epidemiology

As explained elsewhere (chapter 2, Mangen et al. 2005a, Havelaar et al. 2005) epidemiologic studies in the Netherlands lead to a mean estimate of about 80.000 human cases (90% confidence interval between 20.000 and 160.000 cases) of campylobacteriosis per year. As the attributive fraction of chicken meat lies between 20 and 40%, between 16.000-32.000

cases are estimated to be caused by the consumption of chicken meat. A fraction of these will be the consequence of the consumption of cross-contaminated salad. Therefore the estimate of more than 12000 cases, resulting from the baseline model, is rather high. However, given the uncertainty of the assessed exposure distribution, and the uncertainty of the dose-response relationship, especially at low doses, this rather high estimate is not surprising. A similar high estimate was found in a risk assessment of STEC O157 in steak tartare in the Netherlands (Nauta et al. 2001), where doses of only one cfu were predicted to be frequent as well, but the largest number of cases was associated with higher doses.

5.7 Gaps in knowledge

As discussed in previous parts of this chapter, there is quite some uncertainty attending the risk assessment described in this report. Representative quantitative data are scarce and the effects of processing steps and interventions in daily life practice are not well known. In this study we used the best information available (to our knowledge) and asked for expert opinion where adequate data were lacking.

To decrease the uncertainty, data collection should be focused more on quantitative data. Currently much effort is put in collecting data on flock prevalences at farms, but these data could only be applied to a very limited extent in the farm phase of the risk model. In comparison, highly relevant quantitative data on animal prevalences and levels of campylobacter in chicken faeces and on birds entering the processing plant (let alone the variability therein) is very scarce. For risk assessment, more research effort needs to be aimed at collecting such quantitative data, including for example seasonal effects. This effort should combine further improvement and standardization of the microbiological counting methodology, as well as the statistical methods to interpret these data. For quantitative risk assessment, improved methodology to separate variability and uncertainty in the analysis of count data would be very useful.

In the production chain more quantitative data on the effect of processing steps could be helpful to obtain more precise estimates of the model parameter values now estimated by expert judgement. Here, better knowledge on particularly the stages defeathering, cutting and storage at refrigerator temperatures is important.

For the consumer phase of the model, data on actual daily life practices of consumers are preferred above data on statements about behaviour. At least the relationship between what people say and what people do should me made more transparent. In combination with the need to more precisely assess the potentials of risk intervention at the consumer phase, transdisciplinary research in this area involving social scientists, microbiologists and risk modellers is required. Such research has recently started in the Netherlands (Fischer et al. 2005).

The last important step in the model is the dose-response relationship. As low doses are frequent, a better insight in the effects of low doses in different substrates (milk, chicken, salad) would be desirable. There seems to be no reason to assume that the currently available dose-response relationship are representative for exposures as assessed in farm to fork models

as those presented in this report. Also, as also indicated in chapter 2, more knowledge on the effects of acquired immunity to Campylobacter is needed to understand the discrepancy between the predicted exposure rates and the cases of campylobacteriosis estimated from epidemiological data.
A final, general 'gap in knowledge' which requests additional scientific research is quantitative risk modelling itself. One of the findings of the CARMA project, like other international QMRA projects, is that it takes a major investment in time and resources to do a risk assessment, while the result does not solve all uncertainties that exist. Further development of methods to simplify QMRA, yet keeping the crucial complexities aboard, is necessary. One of the possibilities here is to look back on the CARMA risk model (and related models developed elsewhere) and study why which modelling details are essential, where simplified methods could have been applied, and how these can be identified in future risk assessments. For Campylobacter risk assessment, a next step could be to aim for a user friendly model interface that can be used at an international scale.

5.8 Model and Methodology

The risk model is constructed applying MPRM (Modular Process Risk Model) methodology. For this study a combined basic process model is developed, which integrates cross-contamination and removal. It is applied for industrial processing and, in a simpler version, for the cutting stage. The model incorporates some simple mechanistics and is a non-linear model (see Nauta et al. (2005)). It shows that removal is the dominant effect for units (carcasses) contaminated with relatively high numbers of campylobacters, and cross-contamination is dominant for units with relatively low numbers. Hence, the variability in the numbers between units decreases. Along with the inclusion of both campylobacters òn the exterior and ìn the faeces as distinct sources of contamination, the structural application of this non-linear model is a novelty is process risk modelling. It yields results that cannot be obtained by models based on linear relationships only. The latter has been the approach of previous risk assessments of campylobacter, which are based on some count data of chicken processing and linear relationships between the means of log concentrations of campylobacter over the processing stages (e.g. Rosenquist et al. (2003)). The advantage of such an approach is that it is based on actual data, and may thus seem to be a more realistic representation of the actual ('present') situation. However, the disadvantage is that it may improperly model the dynamics of cross-contamination when other levels of contamination apply. As a consequence it may incorrectly assess the effects of interventions, and thus be less suitable for risk management (see Nauta et al. (2005)).
The model does assume linearity for inactivation and removal. This means that the log reduction due to storage, low and high temperature, wash off and decontamination is the same, independent of the level of contamination of the product. This may not be the case. It is known that attachment of Campylobacter to the chicken surface may occur. There may be different types of Campylobacter on the meat, with different attachment capacity and different survival or inactivation dynamics. As a consequence the effects of two inactivation

steps may not sum up. Also, it is known that Campylobacter can occur in different states, 'normally' viable, coccoid and a sublethal (sometimes called 'viable non culturable') state (e.g. Koenraad et al. 1997). This may also have profound impact on the survival dynamics. However, by a lack of adequate quantitative data on these issues, we choose a simplified, linear approach, as usually adopted in QMRA.
The model is implemented as a Monte Carlo spreadsheet model. Including two relevant levels of variability (see section 4.3), it is a rather large computer model, which allows only a limited number of iterations. This means that two independent runs of the model will not give exactly the same result. For the baseline model the predicted number of cases may therefore vary by a few (< 3) percent. This problem gets more relevant when the levels of campylobacter and the exposure are low (for example after intervention). The risk estimate is then based on only a limited number of positive exposures, and thus less precise. However, compared to the total uncertainty attending the model, the imprecision of the estimates thus obtained is small.
Finally, from the calculations it follows that occasional high levels of campylobacter may lead to higher doses and have a large impact on the final risk estimate. Therefore, the (right hand) tails of the (lognormal and other) distributions are important. These tails are a consequence of the precise distributions applied, which may be based on limited data sets, with little data on these tails. This may be an important source of error for the final risk estimate. Overall, rare events (like disturbance of industrial processing, unusual consumer behaviour) may in practice lead to quite some exposure to Campylobacter. Such potentially relevant events are not documented and cannot be included in a risk model as the one presented here. Therefore, further development of risk models aiming at this aspect is needed.

5.9 Conclusions

A risk assessment of Campylobacter in broiler chicken meat in the Netherlands has been described in this report, together with an analysis of the relative importance of this source of campylobacteriosis.
From the baseline model, representing the most likely situation for broiler chicken meat produced in the Netherlands in 2000, from birds reared in Dutch farms, it can be concluded that on average there is a continuous decrease in the level of Campylobacter on the carcasses and meat product. However, variability between flocks is large, and increases in level may also occur. Carcasses are contaminated by campylobacters on the exterior and in the faeces of the birds entering the processing plant. The effects of cutting the carcass and storage of the meat may be considerable, but are also very uncertain. These processes require more research. As consumer behaviour is very variable and data on consumer behaviour and the effect of that behaviour on the microorganisms is scarce, exposure is difficult to assess. The model predicts that most exposures will be low, only one or two cfu. The latter seems to be a rather robust prediction, as with current insight it is hard to imagine how to predict otherwise. Interventions seem to be most effective in the processing plant. At farm level one should strive for further improved hygiene, as this reduces the risk and simplifies scheduled

treatment. Furthermore, if farm hygiene gets too little attention, this could lead to higher levels of contamination of the birds, which may have serious impact on the human risk. In the processing plant, a combined intervention strategy aiming at the campylobacters in the faeces (by phage therapy or the reduction of faecal leakage) and decontamination (chemical or otherwise) at some stage after evisceration is most promising.

In the risk model it is found that interventions aiming at a lower concentration of campylobacter can be very effective, and more efficient than aiming at the prevalence (at flock level, animal level or product level). A similar conclusion was drawn from the risk assessment of campylobacter in broiler flocks in Denmark (Rosenquist et al. 2003).

One to two log reduction by some form of decontamination can lead to more than 80% risk reduction. This reduction may not be seen if products are only tested for presence or absence of Campylobacter at the end of processing or at retail, but it has a strong impact at the level of exposure and probability of illness. The (simplified) explanation for this is that the dose-response curve is approximately linear at low doses. One log reduction in exposure will thus lead to approximately 90% less cases. To achieve the same effect by lowering the prevalence only, the prevalence should be lowered by 90%. This probably will be more difficult to realize than lowering the concentration.

Finally, at the end of this report, the reader should realize that the risk model presented is indeed a model, purposely a much simplified representation of reality constructed with the aim to gain insight in complex processes and to assess and compare the impact of a set of potential control measures to reduce the incidence of human campylobacteriosis in the Netherlands. Here, qualitative outcomes are more relevant than the precise numbers resulting from the quantitative analysis. The authors realize this model lacks many aspects of reality that may be more relevant than assumed in the modelling approach. However, using the best available knowledge, in a project in which governmental risk managers and stakeholder from industry and other parties were actively involved, the model presented may be considered a well structured and helpful tool for risk management decisions, and a handle for further research to control campylobacter.

References

Anderson, S., Christensen, B.B., Fazil, A., Hartnett, E., Lammerding, A., Nauta, M., Paoli, G., and Rosenquist, H., 2003. A draft risk assessment of Campylobacter ssp. in broiler chickens. Joint FAO/WHO activities on risk assessment of microbiological hazards in foods - Interpretative summary - , WHO/FAO.

Anonymous, 2001. Hazard Identification, hazard identification and exposure assessment of Campylobacter spp. in broilers. FAO / WHO, Rome / Geneva.

Anonymous, 2003. Opinion of the Scientific Committee on Veterinary Measures Relating to Public Health On The Evaluation of Antimicrobial Treatments for Poultry Carcasses. European Commission, Health & Consumer Protection Directorate-General.

Bashor, M.P., Curtis, P.A., Keener, K.M., Sheldon, B.W., Kathariou, S., and Osborne, J.A., 2004. Effects of carcass washers on Campylobacter contamination in large broiler processing plants. Poult Sci 83: 1232-9.

Belongia, E.A., Chyou, P.H., Greenlee, R.T., Perez-Perez, G., Bibb, W.F., and DeVries, E.O., 2003. Diarrhea incidence and farm-related risk factors for Escherichia coli O157:H7 and Campylobacter jejuni antibodies among rural children. J Infect Dis 187: 1460-8.

Berrang, M.E., Buhr, R.J., Cason, J.A., and Dickens, J.A., 2002. Microbiological consequences of skin removal prior to evisceration of broiler carcasses. Poult Sci 81: 134-8.

Berrang, M.E. and Dickens, J.A., 2000. Presence and level of Campylobacter spp. on broiler carcasses throughout the processing plant. Journal of Applied Poultry Research 9: 43-47.

Berrang, M.E., Ladely, S.R., and Buhr, R.J., 2001. Presence and level of Campylobacter, coliforms, Escherichia coli, and total aerobic bacteria recovered from broiler parts with and without skin. J Food Prot 64: 184-8.

Bhaduri, S. and Cottrell, B., 2004. Survival of cold-stressed Campylobacter jejuni on ground chicken and chicken skin during frozen storage. Appl Environ Microbiol 70: 7103-9.

Black, R., Levine MM, Clements ML, Hughes TP, and Blaser MJ, 1988. Experimental *Campylobacter jejuni* infection in humans. . Journal of Infectious Diseases 157: 472-479.

Bogaardt, M.J., 2005. Maatschappelijke acceptatie van maatregelen tegen Campylobacter in kippenvlees. Een onderzoek naar de houding van vleeskuikenhouders, pluimveeslachterijen en consumenten in Nederland ten aanzien van mogelijk te nemen maatregelen om de besmetting van kippenvlees met Campylobacter te verminderen. LEI, Den Haag.

Bouwknegt, M., van de Giessen, A.W., Dam-Deisz, W.D.C., Havelaar, A.H., Nagelkerke, N.J.D., and Henken, A.M., 2004. Risk factors for the presence of Campylobacter ssp. in Dutch broiler flocks. Preventive Veterinary Medicine 62: 35-49.

Chan, K.F., Le Tran, H., Kanenaka, R.Y., and Kathariou, S., 2001. Survival of clinical and poultry-derived isolates of Campylobacter jejuni at a low temperature (4 degrees C). Appl Environ Microbiol 67: 4186-91.

Chen, Y., Jackson, K.M., Chea, F.P., and Schaffner, D.W., 2001. Quantification and variability analysis of bacterial cross- contamination rates in common food service tasks. J Food Prot 64: 72-80.

Cogan, T.A., Slader, J., Bloomfield, S.F., and Humphrey, T.J., 2002. Achieving hygiene in the domestic kitchen: the effectiveness of commonly used cleaning procedures. J Appl Microbiol 92: 885-92.

Cooke, R.M., Nauta, M.J., Havelaar, A.H., and Van der Fels, H.J., 2004. Probabilistic

inversion for chicken processing lines. Proceedings of the Conference on Sensitivity Analysis of Model Output. Los Almos, New Mexico.

Corry, J.E. and Atabay, H.I., 2001. Poultry as a source of Campylobacter and related organisms. J Appl Microbiol 90: 96S-114S.

Corry, J., James C, O'Neill DO, Yaman H, Kendall A, and Howell M, 2003. Physical methods, readily adapted to existing commercial processing plants, for reducing numbers of campylobacters on raw poultry. Int J Med Microbiol 293: 32.

Cudjoe, K.S. and Kapperud, G., 1991. The effect of lactic acid sprays on Campylobacter jejuni inoculated onto poultry carcasses. Acta Vet Scand 32: 491-8.

Curtis, L.M., Patrick, M., and Blackburn, C.D., 1995. Survival of Campylobacter jejuni in foods and comparison with a predictive model. Lett Appl Microbiol 21: 194-7.

De Wit, M., Koopmans, M., Kortbeek LM, Wannet WJB, Vinjé J, Leusden F van, Bartelds AIM, and Duynhoven van YTHP , 2001. Sensor, a population-based cohort study on gastroenteritis in the Netherlands: incidence and aetiology. Am J Epidemiol 154: 666-74.

Doorduyn, Y., Brandhof, van den W.E., Duynhoven van Y.T.H.P., Wagenaar J.A., and Pelt, van W., in prep a. Risk factors for endemic *Campylobacter jejuni* infections in the Netherlands: a case-control study.

Doorduyn, Y., Breukink, J., Brandhof, van den W.E., Duynhoven van Y.T.H.P., Wagenaar J.A., and Pelt, van W., in prep b. Risk factors for endemic *Campylobacter coli* infections in the Netherlands.

Evans, M.R., Roberts, R.J., Ribeiro, C.D., Gardner, D., and Kembrey, D., 1996. A milk-borne Campylobacter outbreak following an educational farm visit. Epidemiology and Infection 117: 457-462 .

Evers, E.G., 2004. Predicted quantitative effect of logistic slaughter on microbial prevalence. Prev Vet Med 65: 31-46.

Evers, E.G., Van der Fels, H.J., Nauta, M.J., Schijven, J.F., and Havelaar, A.H., 2004. Het relatieve belang van Campylobacter transmissieroutes op basis van blootstellingsschatting. RIVM rapport 250911003, Bilthoven, the Netherlands.

Farkas J, 1996. Status and prospects of decontamination and preservation of poultry meat / carcasses by ionizing radiation. In: COST Action 97, Pathogenic micro-organisms in poultry and eggs, 7. Status and prospects of decontamination and preservation of poultry and egg products (Colin P, Mulder RWAW, Eds.), p. 75-82. Working Group 3, Proceedings of a workshop, Ploufragan, France, 25-26 November 1996.

Farkas, J., 1998. Irradiation as a method for decontaminating food. A review. Int J Food Microbiol 44: 189-204.

Fazil, A.M., Lowman, R., Stern, N., and Lammerding, A., 1999. Quantitative Risk assessment model for Campylobacter jejuni in chicken. 10th International Workshop on CHRO. abstract CF10, pp 65.

Federighi, M., Cappelier J-M, and Rossero A, 1996. Effect of Avgard™ decontamination process on reduction of thermophilic Campylobacters on chicken carcasses. In: COST Action 97, Pathogenic micro-organisms in poultry and eggs, 7. Status and prospects of decontamination and preservation of poultry and egg products (Colin P, Mulder RWAW, Eds.), p. 125-128. Working Group 3, Proceedings of a workshop, Ploufragan, France, 25-26 November 1996.

Fischer, A.R.H., De Jong, A.E.I., De Jonge, R., Frewer, L.J., and Nauta M.J., 2005. Improving food safety in the domestic environment: the need for a transdisciplinary approach. Risk Analysis in press.

Gezondheidsraad, 1988. Campylobacter jejuni infecties in Nederland.

Hafez, H.M., 1999. Poultry meat and food safety: pre- and post-harvest approaches to reduce

foodborne pathogens. Worlds Poultry Science Journal 55: 269-280.
Hartnett, E., 2001. Human infection with Campylobacter spp. from chicken consumption: a quantitative risk assessment (PhD thesis). University of Strathglyde, Glasgow, UK.
Hartnett, E., Kelly, L.A., Gettinby, G., and Wooldridge, M., 2002. A quantitative risk assessment for campylobacter in broilers: work in progress. International Biodeterioration & Biodegradation 50: 161-165.
Havelaar, A.H., 2001. Campylobacteriose in Nederland; Risico's en interventiemogelijkheden. RIVM rapport 250911001, Bilthoven, the Netherlands.
Havelaar, A.H., Evers, E.G., and Nauta, M.J., 2004. Het effect van logistiek slachten en/of een kiemreducerende behandeling op de besmetting van kippenvlees met Campylobacter. RIVM rapport 250911002, Bilthoven, the Netherlands.
Havelaar, A.H., Nauta, M.J., Mangen, M.-J.J., de Koeijer, A., Evers, E.G., Jacobs-Reitsma, W.F., Bogaardt, M.-J., and Wagenaar, J.A., 2005. Kosten en baten van Campylobacter bestrijding in Nederland; Integratie van risico-analyse, epidemiologie en economie. RIVM rapport 2509011008, Bilthoven, the Netherlands.
Havelaar, A., de Wit, M., and van Koningsveld, R., 2000. Health burden in the Netherlands (1990-1995) due to infections with thermophilic *Campylobacter* species. RIVM rapport 284550004, Bilthoven, the Netherlands.
Izat, A.L., Gardner, F.A., Denton, J.H., and Golan, F.A., 1988. Incidence and level of *Campylobacter jejuni* in broiler processing. Poultry Science 67: 1568-1572.
Jacobs-Reitsma, W., Nauta, M.J., and et al., in prep. Campylobacter counts st several broiler chicken processing stages.
James, C., 2004. Review of meat decontamination. FRPERC JOB Report (draft) on 25.05.2004, University of Bristol, UK.
Katsma, W.E.A., de Koeijer, A.A., Fischer, E.A.J., Jacobs Reitsma, W.F., and Wagenaar, J.A., 2005. Campylobacter prevalence in broiler flocks in the Netherlands. Modelling transmission within and between flocks and efficacy of interventions. Animal Sciences Group (ASG)Wageningen-UR. Report ASG05/I00113.
Keener, K., Bashor MP, Curtis PA, Sheldon BW, and Kathariou S, 2004. Comprehensive Review of Campylobacter and Poultry Processing. Comprehensive Reviews in Food Science and Food Safety 3: 105-116.
Kist, M., 2002. Food-borne Campylobacter infections. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 45: 497-506.
Kistemaker, C., Bouman, M., and Hulshof, K., 1998. De consumptie van afzonderlijke producten door Nederlandse bevolkingsgroepen - Voedselconsumptiepeiling 1997-1998. 1998; . TNO-rapport V98.812, TNO Voeding The Netherlands.
Koenraad, P.M.F.J., Rombouts, F.M., and Notermans, S.H.W., 1997. Epidemiological aspects of thermophilic Campylobacter in water-related environments: A review. Water Environment Research 69: 52-63.
Koidis, P. and Doyle, M.P., 1983. Survival of Campylobacter jejuni in the presence of bisulfite and different atmospheres. Eur J Clin Microbiol 2: 384-8.
Kusumaningrum, H.D., van Asselt, E.D., Beumer, R.R., and Zwietering, M.H., 2004. A quantitative analysis of cross-contamination of Salmonella and Campylobacter spp. via domestic kitchen surfaces. J Food Prot 67: 1892-903.
Lindqvist, R., Sylven, S., and Vagsholm, I., 2002. Quantitative microbial risk assessment exemplified by Staphylococcus aureus in unripened cheese made from raw milk. Int J Food Microbiol 78: 155-70.
Mangen, M.-J.J., Havelaar, A.H., Nauta, M.J., de Koeijer, A.A., and de Wit G.A., 2005a. Controlling Campylobacter in the chicken meat chain – Cost-effectivity and cost-utility analysis. RIVM report 250911007, Bilthoven, the Netherlands.

Mangen, M.-J.J., Havelaar, A.H., and Poppe, K., 2005b. Controlling Campylobacter in the chicken meat chain – Estimation of intervention costs. Agricultural Economics Institute (LEI), Den Haag. LEI report 6.05.01.

Mead, G., 2004. Campylobacter update - the solution. International Poultry Production 12: 9-11.

Mead, G.C., Hudson, W.R., and Hinton, M.H., 1995. Effect of changes in processing to improve hygiene control on contamination of poultry carcasses with campylobacter. Epidemiology and Infection 115: 495-500.

Medema, G.J., Teunis, P.F., Havelaar, A.H., and Haas, C.N., 1996. Assessment of the dose-response relationship of Campylobacter jejuni. Int J Food Microbiol 30: 101-11.

Montville, R., Chen, Y., and Schaffner, D.W., 2001. Glove barriers to bacterial cross-contamination between hands to food. J Food Prot 64: 845-9.

Moorhead, S.M. and Dykes, G.A., 2002. Survival of Campylobacter jejuni on beef trimmings during freezing and frozen storage. Lett Appl Microbiol 34: 72-6.

Mylius, S.D., Nauta, M.J., and Havelaar, A.H., submitted. Cross-contamination during food preparation: a mechanistic model applied to chicken-borne Campylobacter.

Nauta, M.J., 2000. Separation of uncertainty and variability in quantitative microbial risk assessment models. International Journal of Food Microbiology 57: 9-18.

Nauta, M.J., 2001. A modular process risk model structure for quantitative microbiological risk assessment and its application in an exposure assessment of *Bacillus cereus* in a REPFED. RIVM report 149106007, Bilthoven, the Netherlands.

Nauta, M.J., 2002. Modelling bacterial growth in quantitative microbiological risk assessment: is it possible? Int J Food Microbiol 73: 297-304.

Nauta, M.J., 2005. Microbiological risk assessment models for partitioning and mixing during food handling. International Journal of Food Microbiology in press.

Nauta, M.J., Evers, E.G., Takumi, K., and Havelaar, A.H., 2001. Risk assessment of Shiga toxin producing *Escherichia coli* O157 in steak tartare in the Netherlands. RIVM report 257851003, Bilthoven, the Netherlands.

Nauta, M.J., Van der Fels-Klerx, H.J., and Havelaar, A.H., 2005. A poultry processing model for quantitative microbiological risk assessment. Risk Analysis 25:85-98.

Neijssen, P., 1988a. Levensmiddelendoorstraling. Inleiding tot levensmiddelendoorstraling aan de hand van vaak gestelde vragen. VMT 2-5.

Neijssen, P., 1988b. Levensmiddelendoorstraling (vervolg). Inleiding tot levensmiddelendoorstraling aan de hand van vaak gestelde vragen. VMT 6-8.

Oosterom, J., de Wilde, G.J.A., de Boer, E., de Blaauw, L.H., and Karman, H., 1983. Survival of *Campylobacter jejuni* during poultry processing and pig slaughtering. Journal of Food Protection 46: 702-706.

Puridec, 2004. Understanding the key radiation processing parameters - a guide for food producers. Handout at Isotron conference 'Voedselveiligheid, ook uw prioriteit', 21 september 2004, Ede, The Netherlands.

Redmond, E.C. and Griffith, C.J., 2003. Consumer food handling in the home: a review of food safety studies. J Food Prot 66: 130-61.

Rietveld, H., 2002. De wettelijke aspecten van doorstraling. Presentation at Isotron conference 'Voedselveiligheid, ook uw prioriteit', 21 september 2004, Ede, The Netherlands.

Ritz-Bricaud, M., Nauta, M., Federighi, M., and Havelaar, A., 2003. What part of uncertainty and variability in the modeling of Campylobacter survival in frozen chicken meat? In: J.F.M. van Impe, A.H. Geeraerd, I. Leguérinel and P. Mafart (Eds.), Predictive Modelling in Foods Conference Proceedings, p. 332-334. Katholieke Universiteit Leuven/BioTeC, Belgium.

Rosenquist, H., Nielsen, N.L., Sommer, H.M., Norrung, B., and Christensen, B.B., 2003. Quantitative risk assessment of human campylobacteriosis associated with thermophilic Campylobacter species in chickens. Int J Food Microbiol 83: 87-103.

Sandberg, M., Hofshagen M, Řstensvik Ř, Skjerve E, and Innocent G , Submitted. Campylobacter on frozen broiler carcasses as a function of time.

Slavik, M., Kim J-W, Pharr M.D., Raben D.P/, Tsai S., and Lobsinger C.M., 1994. Effect of Trisodium Phosphate on Campylobacter Attached to Post-Chill Chicken Carcasses. Journal of Food Protection 57: 324-326.

Smith, S., Dunbar, M., Tucker, D., and Schaffner, D.W., 2003. Efficacy of a commercial produce wash on bacterial contamination of lettuce in a food service setting. J Food Prot 66: 2359-61.

Snijders, J.M.A., Lipman, L.J.A., and Nedelkovski, R., 2004. Practical germicidal treatment in the poultry processing line. V&V report 0402, Utrecht University, the Netherlands.

Stekelenburg, F.K. and Logtenberg, H., 2004. De ins en outs van decontaminatie van pluimveevlees. TNO-rapport V 5667, Zeist, the Netherlands.

Stern, N.J., Clavero, M.R.S., Bailey, J.S., Cox, N.A., and Robach, M.C., 1995. Campylobacter spp. in broilers on the farm and after transport. Poultry Science 74: 937-941.

Stern, N.J., Hiett, K.L., Alfredsson, G.A., Kristinsson, K.G., Reiersen, J., Hardardottir, H., Briem, H., Gunnarsson, E., Georgsson, F., Lowman, R., Berndtson, E., Lammerding, A.M., Paoli, G.M., and Musgrove, M.T., 2003. Campylobacter spp. in Icelandic poultry operations and human disease. Epidemiol Infect 130: 23-32.

Stern, N., Rothenberg P.J., and Stone J.M., 1985. Enumeration and reduction of Campylobacter jejuni in poultry and red meats. Journal of Food Protection 48: 606-610.

Svetoch, E.A., Stern, N.J., Eruslanov, B.V., Kovalev, Y.N., Volodina, L.I., and et al., 2003. Use of *Bacillus* and *Paenibacillus* produced bacteriocins for therapeutic control of *Campylobacter jejuni* in chickens. International Journal of Medical Microbiology 293: 26-27.

Teunis, P., Van den Brandhof, W., Nauta, M., Wagenaar, J., Van Pelt, W., and Van den Kerkhof, H., 2005. A reconsideration of the Campylobacter dose-response relation. Epidemiology and Infection in press.

Teunis, P.F. and Havelaar, A.H., 2000. The Beta Poisson dose-response model is not a single-hit model. Risk Analysis 20: 513-20.

Teunis, P.F., Nagelkerke, N.J., and Haas, C.N., 1999. Dose-response models for infectious gastroenteritis. Risk Anal 19: 1251-60.

Uyttendaele, M., De Troy, P., and Debevere, J., 1999. Incidence of Salmonella, Campylobacter jejuni, Campylobacter coli, and Listeria monocytogenes in poultry carcasses and different types of poultry products for sale on the Belgian retail market. J Food Prot 62: 735-40.

Van den Brandhof, W., Wagenaar, J., and Van den Kerkhof, H., 2003. An outbreak of campylobacteriosis after drinking pasteurized milk, 2002, The Netherlands. International Journal of Medical Microbiology 293 (S35): 142.

Van der Fels-Klerx, H.J., Goossens, L.H.J., Nauta, M.J., Cooke, R.M., and Havelaar, A.H., 2005. A structured expert judgment study for microbiological risk assessment on campylobacter transmission during broiler chicken processing . Risk Analysis 25:109-124.

Van der Zee, H., Wit, B., and De Boer, E., 2002. Monitoring pathogenen in kip en kipproducten. Keuringsdienst van Waren Oost, afd. Signalering, Zutphen, The Netherlands.

Van Netten, P., Huis in 't Veld J, and Mossel D.A.A., 1994a. An in-vitro meat model for the immediate bactericidal effect of lactic acid decontamination on meat surfaces . Journal of Applied Bacteriology 76: 49-54.

Van Netten, P., Huis in 't Veld J.H.J., and Mossel D.A.A., 1994b. The immediate bactericidal effect of lactic acid on meat-borne pathogens. Journal of Applied Bacteriology 77: 490-496.

Van Pelt, W. and Valkenburg, S.M., 2001. Zoonoses and zoonotic agents in humans, food, animals and feed in the Netherlands . Keuringsdienst van Waren, RIVM.

Vellinga, A. and Van Loock, F., 2002. The dioxin crisis as 'experiment' to determine poultry related Campylobacter enteritis. Emerging Infectious Diseases 8: 19-22.

Vose, D., 2000. Risk Analysis: A quantitative guide. 2nd ed. John Wiley & Sons, Chichester.

VVDO, 1998. Decontaminatie van pluimveevlees. Rapport 97.01, Universiteit Utrecht.

Wagenaar, J., Van Bergen, M., Mueller, M., Monie, K., and Carlton, R., 2001. Phage therapy of Campylobacter jejuni colonisation in broilers. poster CHRO .

Wassenaar, T., Van der Wal, F.J., and Wagenaar J., 2004. De typering van Campylobacter en de relatie tussen Campyloacter type en virulentie. Rapport nr ASG04/0010255, Animal Sciences Group Wageningen UR, Lelystad.

WHO, 1997. Food irradiation sky's the limit. Press Release WHO/68.

WHO/FAO, 1988. Food irradiation. A technique for preserving and improving the safety of food.

Whyte, P., Collins, J.D., McGill, K., Monahan, C., and O'Mahony, H., 2001. Quantitative investigation of the effects of chemical decontamination procedures on the microbiological status of broiler carcasses during processing. J Food Prot 64: 179-83.

Whyte, P., McGill, K., and Collins, J.D., 2003. An assessment of steam pasteurization and hot water immersion treatments for the microbiological decontamination of broiler carcasses. Food Microbiology 20: 111-117.

Worsfold, D. and Griffith, C.J., 1997. Assessment of the standard of consumer food safety behavior. Journal of Food Protection 60: 399-406.

Acknowledgements

The study described in this report would not have been realized without the help of a lot of people.
The following people and teams are gratefully acknowledge for their contributions:
Hanne Rosenquist (DFVF, Denmark)
Janet Corry (University of Bristol, UK)
FAO/WHO drafting group 'Risk assessment of Campylobacter in broiler chickens' (Anderson et al. 2003)
Decisionalysis Risk Consultants Inc. (Ottawa, Canada)
Peter Enthoven, (CCL-Research)
Jaap Obdam, (Plukon Poultry, Wezep)
The expert panel consulted for the expert judgement processing model (Van der Fels-Klerx et al. 2005)
Jos van de Nieuwelaar (Stork)
Willem Heemskerk (Meyn)
Roger Cooke (Technical University Delft)
Louis Goossens (Technical University Delft)
Ratko Nedelkovski (IRAS, Utrecht University)
Jos Snijders (IRAS, Utrecht University)
Ine van der Fels-Klerx (RIVM, now at RIKILT, Wageningen University))
Sido Mylius (RIVM)
Peter Teunis (RIVM)
Yvonne Doorduyn (RIVM)
Gert Steentjes (RIVM)
Martine Bakker (RIVM)
Annemarie Pielaat (RIVM)
Anne Mensink (RIVM)
CARMA industry forum
CARMA project group
CARMA steering committee

Appendix

Summary of expert judgement results

The parameter values of the industrial processing model applied in the baseline model are the median values of a set of 500 samples of the uncertainty distributions obtained from the expert judgement study described by Van der Fels-Klerx et al. (2005) and Cooke et al. (2004). Results of a larger set of 10.000 samples are given in table A1. (Due to the differences in sample size median values may differ from the values given in table 3.14.) For the five transfer coefficient distributions are illustrated in fig A1. As most distributions are skewed, the horizontal axis is represented on a log scale. The median is considered to be more representative for the average of the distribution than the mean.

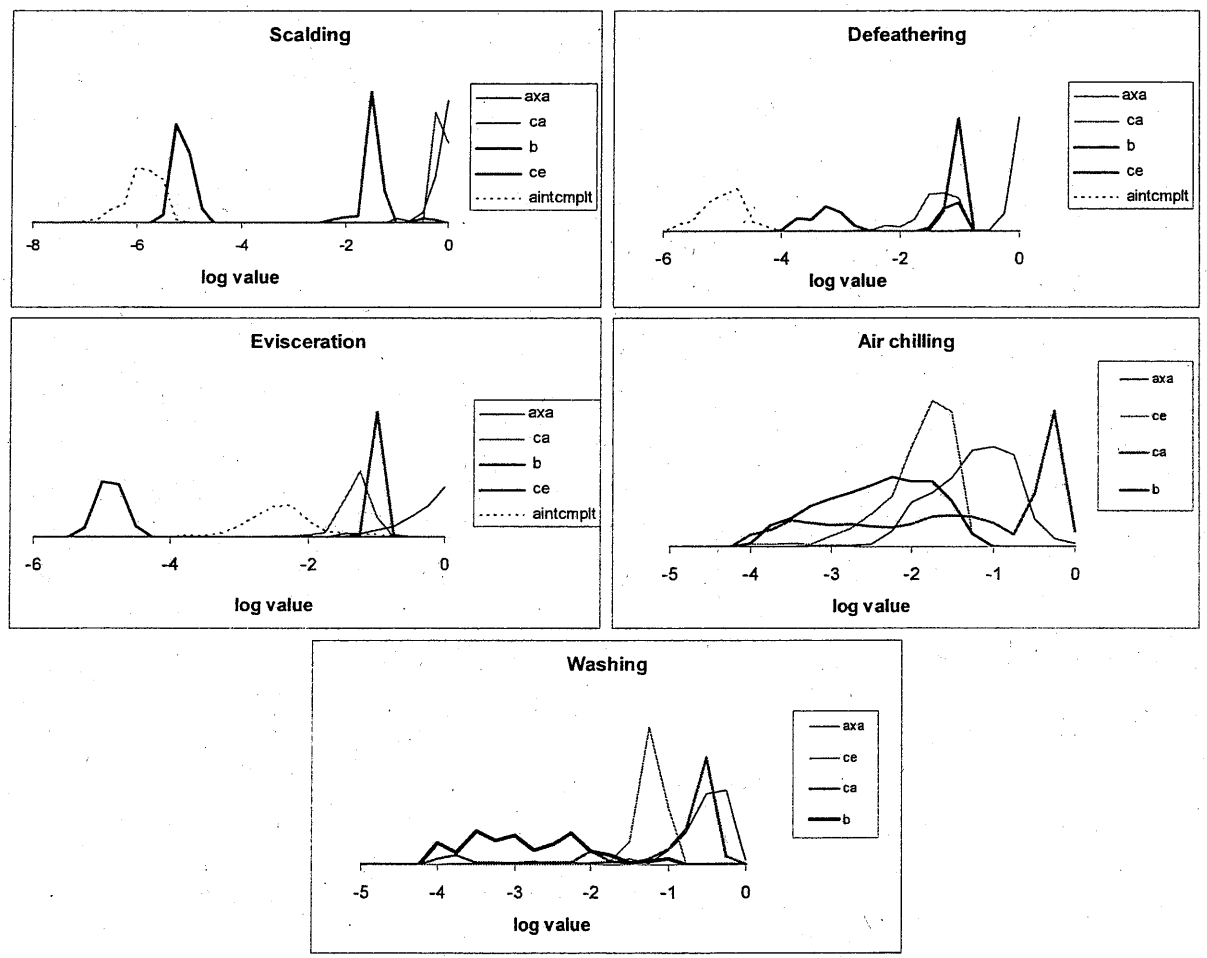

Figure A1. The uncertainty distributions of the processing parameters a_{ext} (axa) c_{ext} (ca), b_{env} (b), c_{env} (ce), and 1- a_{fec} (aintcmplt) for the five processing stages, resulting from the probablistic inversion on the expert estimates.

Correlations between parameter values are included in samples of sets of parameter values resulting from probablistic inversion. Correlation can be included in the model analysis of the uncertainty by running the model for random sets of samples, as e.g. in the uncertainty analysis leading to fig 5.1. These correlations are not mentioned here.

Table A1. Summary of the results of the expert judgement study for industrial broiler chicken processing.
The mean, standard deviation and 5, 50 and 95 percentiles of the model parameter estimates express the uncertainty of the global optimized decision maker, resulting from a set of 10,000 samples after probablistic inversion.

		a_{ext}	c_{ext}	b_{env}	c_{env}	1-a_{fec}	$m_{s\,\mu}$	p_{fec}
scalding	mean	0.760	0.715	8.37E-06	0.052	1.59E-06	1.97	0.495
	sd	0.232	0.138	3.23E-06	0.078	1.06E-06	0.66	0.196
	0.05	0.222	0.534	4.46E-06	0.012	3.41E-07	1.02	0.207
	0.50	0.848	0.714	7.13E-06	0.036	1.42E-06	2.00	0.493
	0.95	0.965	0.944	1.48E-05	0.166	2.63E-06	3.00	0.800
defeathering	mean	0.855	0.050	3.09E-02	0.101	1.34E-05	1.72	0.675
	sd	0.145	0.028	3.78E-02	0.025	1.17E-05	0.65	0.147
	0.05	0.648	0.007	1.60E-04	0.049	2.51E-06	1.02	0.602
	0.50	0.904	0.048	1.11E-03	0.113	1.03E-05	2.02	0.698
	0.95	0.983	0.092	9.78E-02	0.124	2.95E-05	2.98	0.800
evisceration	mean	0.464	0.040	1.08E-05	0.084	6.23E-03	1.72	0.668
	sd	0.292	0.017	4.77E-06	0.009	1.16E-02	0.65	0.147
	0.05	0.040	0.016	5.00E-06	0.070	6.03E-04	1.00	0.400
	0.50	0.450	0.040	1.00E-05	0.085	2.95E-03	2.00	0.693
	0.95	0.940	0.065	2.09E-05	0.095	2.51E-02	2.98	0.800
washing	mean	0.335	0.216	7.18E-03	0.062			
	sd	0.210	0.151	1.82E-02	0.020			
	0.05	0.003	0.000	1.25E-04	0.026			
	0.50	0.295	0.262	1.24E-03	0.061			
	0.95	0.664	0.360	3.73E-02	0.096			
chilling	mean	0.099	0.221	9.22E-03	0.017			
	sd	0.114	0.258	1.20E-02	0.012			
	0.05	0.008	0.000	2.49E-04	0.002			
	0.50	0.063	0.054	4.28E-03	0.016			
	0.95	0.300	0.641	3.51E-02	0.037			