CAMPYLOBACTER RISK MANAGEMENT AND ASSESSMENT

CARMA

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Controlling Campylobacter in the chicken meat chain

Towards a decision support model

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LEI WAGENINGEN UR

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Abstract

The goal of the CARMA project is to advise the Dutch government on the effectiveness and efficiency of measures aimed at reducing campylobacteriosis in the Dutch population. This report describes the framework of the CARMA project. Components forming the project are a chicken meat risk model, intervention measures in chicken meat production, autonomous developments, economic analysis, the societal acceptability of the intervention measures and the political culture in which the decision making takes place. The risk model is used here to estimate the effects of interventions in the chicken meat chain, from farm to consumer. The output of the risk assessment model, in terms of number of expected Campylobacter infections per age group per period, is input for the economic analysis. Autonomous developments that may affect risks in the near future are concentration in the production chain, increasing consumption of chicken meat and increasing away-from-home consumption. The economic evaluation focuses on the cost per case (i.e. Campylobacter infection) averted and the cost per (quality-adjusted) life year gained. The effectiveness of the interventions also depends on the acceptability of the interventions to stakeholders (industry, retailers and consumers). There are differences in the role that economic evaluation plays in the decision making of the two Dutch Ministries (Agriculture and Public Health) involved.

Preface

Campylobacter infections pose a serious public health problem in the Netherlands. Chicken may be responsible for up to 40% of all human cases of campylobacteriosis. Several intervention measures are available to reduce the contamination of chicken meat and thereby significantly reduce the incidence of human infections with Campylobacter. For advice on the effectiveness and efficiency of measures aimed at reducing campylobacteriosis in the Dutch population, the Dutch government finances the so-called CARMA (**Ca**mpylobacter **R**isk **M**anagement and **A**ssessment) project that started in 2001. The CARMA project is a collaboration between the National Institute for Public Health and the Environment (RIVM), the Animal Sciences Group-Lelystad, the Agricultural Economics Research Institute (LEI), the Inspectorate for Health Protection and Veterinary Public Health (KvW) and RIKILT - Institute of Food Safety. One of the products of the CARMA project is to deliver relevant information to support the public decision making process. This report presents information about effectiveness, efficiency, legitimacy and present risk culture of measures aimed at reducing campylobacteriosis in the Dutch population. Special thanks go to the Steering Committee of the CARMA-project, especially Wieke Galama (LNV), Jaap Jansen and Rob van Oosterom (VWA), Rosanne Metaal (VWS), and Dr. Krijn Poppe (LEI), for their comments on earlier versions of this report. We also would like to thank Dr. Tanya Roberts (Economic Research Service, United States Department of Agriculture), Dr. Alison Burrell (Wageningen University), Dr. André Ament (University of Maastricht) and Dr. Annet Velthuis (Wageningen University) for reviewing a draft of this report.

More information on the CARMA project can be found at the website www.rivm.nl/carma.

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Samenvatting

Infecties met bacteriën van het geslacht Campylobacter vormen een belangrijk volksgezondheidsprobleem in Nederland. Tot 40 procent van de gevallen van humane campylobacteriose wordt veroorzaakt door de consumptie van besmet kippenvlees. Er zijn verschillende interventies in de productieketen mogelijk om de besmetting van kippenvlees te verminderen. Deze interventies kunnen bijdragen aan een verminderde incidentie van humane campylobacteriose. Het doel van het CARMA (**Ca**mpylobacter **R**isk **M**anagement and **A**ssessment) project is om de overheid te adviseren over de effectiviteit en doelmatigheid van interventies gericht op het reduceren van campylobacteriose in de Nederlandse bevolking. Dit rapport beschrijft het raamwerk van het CARMA project: elke fase van het onderzoek wordt beschreven in relatie tot de andere fasen van het onderzoek. De belangrijkste onderdelen van het onderzoek zijn: de ontwikkeling van een risicomodel voor kippenvlees, definitie van interventiemaatregelen in de productieketen van kippenvlees, onderzoek naar de aanvaardbaarheid van deze maatregelen, economische evaluatie, onderzoek naar autonome ontwikkelingen en onderzoek naar de politieke cultuur omtrent besluitvorming ten aanzien van voedselveiligheid. In elk van deze delen van het onderzoek worden keuzes gemaakt ten aanzien van bijvoorbeeld de tijdspanne van het onderzoek, welke factoren wel en niet in de modellen worden meegenomen, de interpretatie van termen en definities, onzekerheid en variabiliteit in de modellen, enzovoorts. Doel van dit rapport is om de gemaakte keuzes te expliciteren.

Het risicomodel voor kippenvlees zal gebruikt worden om de effecten van interventies in de productieketen, van de boerderijniveau tot en met de verwerking bij de consument thuis, te schatten. Het model beschrijft daartoe de blootstelling van de Nederlandse consument aan *Campylobacter* spp. via kippenvlees en vervolgens het daarmee samenhangende gezondheidsrisico. Het model wordt in eerste instantie gericht op kipfilet. De effecten van interventie in de primaire productie, bij het slachten, ten aanzien van consumentengedrag en van geïmporteerd vlees zullen worden vergeleken met de status-quo in het basisjaar 2000. De uitkomsten van het risicomodel, het verwachte aantal infecties per leeftijdsgroep en per periode, vormt de invoer van het economische model.

Autonome ontwikkelingen die in de nabije toekomst zullen plaatsvinden worden niet door de overheid aangestuurd maar kunnen wel de risicoschatting en de interventiemaatregelen beïnvloeden. Zo vindt er bijvoorbeeld een concentrering plaats in de productieketen van kippenvlees. De gemiddelde grootte van boerderijen, slachthuizen en verwerkende bedrijven neemt toe, terwijl hun aantal recent is afgenomen. De grootste aanvoer van levende kuikens komt uit Nederland, terwijl 10% uit het buitenland komt. De consumptie van kippenvlees is de laatste jaren in Nederland gestegen. Bovendien wordt buitenshuis eten steeds populairder. Een laatste voorbeeld van autonome ontwikkelingen is het toenemende marktaandeel van supermarkten, ten koste van het aantal vrij gevestigde slagers.

De economische evaluatie van interventies zal zowel worden uitgevoerd als een kosten-effectiviteitsanalyse (KEA) als een kosten-utiliteitsanalyse (KUA). De kosten per vermeden geval van campylobacteriose en de kosten per (kwaliteits-gewogen) levensjaar zijn de voornaamste doelvariabelen. Onderzoek naar de kosten van ziekte zal zich richten op directe kosten binnen en buiten het gezondheidszorgsysteem alsmede indirecte kosten buiten dit systeem. Economische evaluatie vindt plaats vanuit een maatschappelijk perspectief is een bestaand onderdeel van de onderbouwing van beleidsbeslissingen van het Ministerie van VWS. Bij het Ministerie van LNV heeft kosteneffectiviteit op maatschappelijk niveau tot op

heden minder aandacht gekregen. Bij dit Ministerie is de aandacht meer gericht op de gevolgen voor de kosten in de productieketen en voor de internationale concurrentiepositie.

De effectiviteit van maatregelen hangt ook af van de acceptatie door belanghebbende groeperingen (industrie, detaillisten, consumenten). Binnen het CARMA project zijn de meningen van belanghebbenden onderzocht. Ook de context waarin beslissingen worden genomen is van belang, inclusief de randvoorwaarden die de Nederlandse regering in acht moet nemen bij het nemen van besluiten.

Summary

Campylobacter infections pose a serious public health problem in the Netherlands. Chicken meat may be responsible for up to 40% of all human cases of campylobacteriosis. Several intervention measures are available to reduce the contamination of chicken meat and thereby significantly reduce the incidence of human infections with Campylobacter. The CARMA (**Ca**mpylobacter **R**isk **M**anagement and **A**ssessment) project has the goal of advising the Dutch government on the effectiveness and efficiency of measures aimed at reducing campylobacteriosis in the Dutch population. This report describes the framework of the CARMA project: each stage of that framework and its relation with other stages. The main stages are the development of a chicken meat risk model, the definition of intervention measures in chicken meat production, a study of autonomous developments, economic analysis of intervention measures, a study of the societal acceptability of the intervention measures and research into the political culture surrounding decision making with regard to reduction of Campylobacter infections. In each step choices are made about time scale, what to include in models as well as in the selection/definition of stakeholders, interpretations of terms and notions, uncertainty and variability in models and trends, etcetera. The aim of this report is to make these choices explicit.

The chicken meat risk model will be used to estimate the effects of interventions in the chicken meat chain, from the farm level to the consumer. The purpose of the model is first to describe the exposure of the Dutch population to *Campylobacter* spp. as a consequence of the consumption of chicken meat, and second to estimate the health risks associated with consumption of chicken meat. The model will first concentrate on risk associated with chicken breasts. The effects of intervention measures concerning primary production, processing, consumer behaviour and imported meats will be assessed in comparison to the status quo in the base year 2000. The output of the risk assessment model, in terms of number of expected Campylobacter infections per age group per period, is input to the economic analysis.

Autonomous developments that will take place in the near future are not steered by the government, but can influence the risk assessment and the intervention measures. For instance, concentration is taking place in the chicken meat production chain. The average size of chicken farms, slaughterhouses and processing plants is increasing, whereas their number has decreased recently. Most of the supply of live chickens comes from the Netherlands itself, and 10% comes from abroad. Dutch consumption of chicken meat has increased over the last years. Furthermore, away-from-home eating is becoming more and more popular in the Netherlands. A final example of an autonomous development is that the market share of supermarkets is growing, while the number of independent butchers has decreased in recent years.

The economic evaluation of interventions to reduce human campylobacteriosis will be in the form of both cost-effectiveness analysis (CEA) and cost-utility analysis (CUA). The cost per case (i.e. infection) averted and the cost per (quality-adjusted) life year gained are major output measures. The cost of illness study will cover direct costs inside and outside the healthcare system, and indirect costs outside the healthcare system. Economic evaluation research from the societal perspective is an issue in decision making of the Ministry of Public Health, albeit not yet in the domain of food safety. At the Ministry of Agriculture, the concept of cost-effectiveness at the societal level has so far received less attention. Here, the focus has mainly been on the consequences of interventions for food production costs and international competitive position of Dutch agricultural produce.

The effectiveness of the interventions also depends on the acceptability of the interventions to stakeholders (industry, retailers and consumers). The CARMA-project gained insight in stakeholders' opinions by conducting a stakeholders analysis. Furthermore, the context in which a risk management decision is made is of importance. The risk culture includes limitations on decision making by the Dutch government.

1 Introduction

1.1 The CARMA project

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

The most important reservoirs of Campylobacter are found among animals, including farm animals, wild animals and pets. These reservoirs continuously contaminate the human environment, including the domestic environment and food products, hereby creating many pathways by which humans can come in contact with Campylobacter. Different research methods have been used, both nationally and internationally, to evaluate the relative importance of different exposure pathways, including case-control studies, microbiological analyses of patients and putative reservoirs, the typing of isolates of different origins, and statistical methods (Havelaar, 2002). Many studies have indicated chicken to be an important source of contamination, but this is by no means the only important contamination route. Other identified risk factors are meat from pigs and cattle, raw milk, direct contact with animals, contaminated surface water, and foreign travel. Drinking water is not important in the epidemiology of Campylobacter in the Netherlands. Little is known about the (relative) quantitative impact of these risk factors. A preliminary estimate, based on limited Dutch data and extrapolation of international data, suggests that chicken is responsible for 40 %, at the most, of all human cases of campylobacteriosis. Other important factors appear to be foreign travel (10-20 %), contact with young dogs (10-20 %) and the consumption of barbecued meat of all kinds (around 10 %). However, these estimates are highly uncertain (Havelaar, 2002).

The poultry industry in the Netherlands and Dutch government reached an agreement on the plans *Plan van Aanpak 1997* and *Actieplan 2000+,* aimed at reducing the contamination of chicken and chicken products with Salmonella and Campylobacter. Subsequently, these plans have been implemented. However, especially the measures with regard to Campylobacter have not been sufficiently effective. In the past years, the prevalence of Campylobacter in chicken and chicken products within retail amounted to more than 30 % (31 % in 2000, 32.5% in 2001, and 31.3 % in 2002). The prevalence of contamination with Salmonella was reduced from 21 % in 2000 to 13.4 % in 2002 (Van der Zee *et al*, 2001, 2002, 2003).

Interventions aimed at reducing the contamination of chicken meat are expected to significantly reduce the incidence of human infections with Campylobacter. The contamination of chicken meat originates from the primary production stage. In recent years, intensified hygienic measures have been implemented in the primary production stage, coinciding with a reduction of the prevalence of contaminated flocks from 48 % in 1998 to 35 % in 2000 (Van Pelt and Valkenburgh, 2001). Additional hygienic measures can be made but are expected to reduce but not eliminate the infection of broilers with Campylobacter. Other intervention measures in primary production, such as reducing the susceptibility to become infected (e.g. by vaccination) and suppressing inadvertently introduced infections, are not expected to be very successful in the near future and are not considered in the project. Hence, additional measures in consequent stages of the food production chain are necessary to further reduce the contamination of chicken meat with Campylobacter. Such measures may include canalisation of contaminated flocks (e.g., logistic slaughtering) and improved hygiene during processing and treatment of the end product (e.g., freezing, decontamination, irradiation, mild heat treatment, drying).

Effective prevention of human campylobacteriosis requires a well-balanced set of measures. To this aim, the CARMA (**Ca**mpylobacter **R**isk **M**anagement and **A**ssessment) project has been started in 2001. The goal of the project is to advise on the effectiveness and efficiency of measures aimed at reducing campylobacteriosis in the Dutch population. This goal is reached by providing scientific support to a risk management process, as defined by the Codex Alimentarius Commission on Food Hygiene (Anonymous, 2001). Risk managers are the Ministry of Health, Welfare and Sports and the Ministry of Agriculture, Nature and Food Quality. This underlying report is intended for risk managers and describes the framework of and the methodology used for the different parts in the CARMA project, and accompanying considerations and choices made by researchers in consultation with the risk managers.

1.2 Design of the CARMA project

Figure 1 shows the general approach of the CARMA project. In the first (completed) phase, all available information was collected and summarised in an extensive risk profile (Havelaar, 2002). This information is used to assess the relative contribution of different sources of contamination to the incidence of human Campylobacter infections. A risk model will be build for each major route of infection, starting with the consumption of chicken meat. A risk model describes the transmission of Campylobacter for the particular contamination route and combines the resulting exposure estimate with dose-response information in order to assess the incidence of Campylobacter infections. In the disease burden model, different outcomes related to these infections, including gastro-enteritis, Guillain-Barré syndrome, reactive arthritis, inflammatory bowel disease and mortality, are quantified. The combined disease burden of these end-points is expressed in Disability Adjusted Life Years (DALYs). Autonomous developments are defined as developments that will take place in the near future (approximately between 2005 and 2010) when no influence with policy is exerted by the government – developments not steered by the government such as societal trends, market mechanisms, unexpected developments (like crises, disasters). These autonomous developments can be of influence on the size and extent in which citizens of the Netherlands get infected and ill due to preparing (e.g. cross-contamination) and eating chicken meat (products) contaminated with Campylobacter, and so on the risk assessment model and on the intervention measures. The economic model evaluates the losses from illnesses due to Campylobacter infections in the starting situation. In consultation with risk managers and stakeholders, a series of potential intervention measures are selected. The effects of these measures on the incidence of infection (risk model), disease burden of related illnesses (disease burden model) and associated losses (economic model) are estimated. In addition, the costs associated with the implementation of intervention measures are evaluated in the economic model. All information collected, including reduced disease burden and its associated savings, as well as costs of interventions to be implemented, are combined in the cost-effectiveness analysis. Here, different interventions are compared based on their (net) costs per case averted and costs per (quality adjusted) life year gained. This allows *a priori* evaluation of different sets of intervention measures. Absolute effects, costs and cost-effectiveness ratios are important elements of information to support risk management decisions. However, societal and political factors also have a major effect on decision-making. Therefore, in the project these factors are also described and presented to decision-makers. The key elements of the CARMA project will be introduced briefly in the remainder of this chapter.

1.3 Decision making process

For making policy on reducing and controlling Campylobacter in the chicken meat chain[1], policymakers of the national government (risk managers) need certain knowledge and information. These risk managers want to know whether policy (measures) will have the desired results, if and what unwanted side-effects of policy will occur, and whether the results will match the expectations of the target groups like chicken meat farmers, processing plants and consumers. Information about these issues is important for risk managers in making a considered choice out of intervention measures by which the contamination of chicken meat can be reduced. A considered choice is important because then the chances can be enhanced that the policy goal of reducing campylobacteriosis in the Dutch population can be realised. That means that measures to be chosen have to be effective, efficient and legitimate. The effectiveness of the interventions depends also on the acceptability of the interventions to stakeholders (industry, retailers and consumers). Furthermore the context, in which a decision concerning risk management is made, is of influence; the so-called risk culture that includes limitations to decision making by the Dutch government. Information on all these aspects will be presented to the risk managers.

[1] The term ‘chicken meat chain’ summarizes all stakeholders in the chain, from the farm level to the consumer.

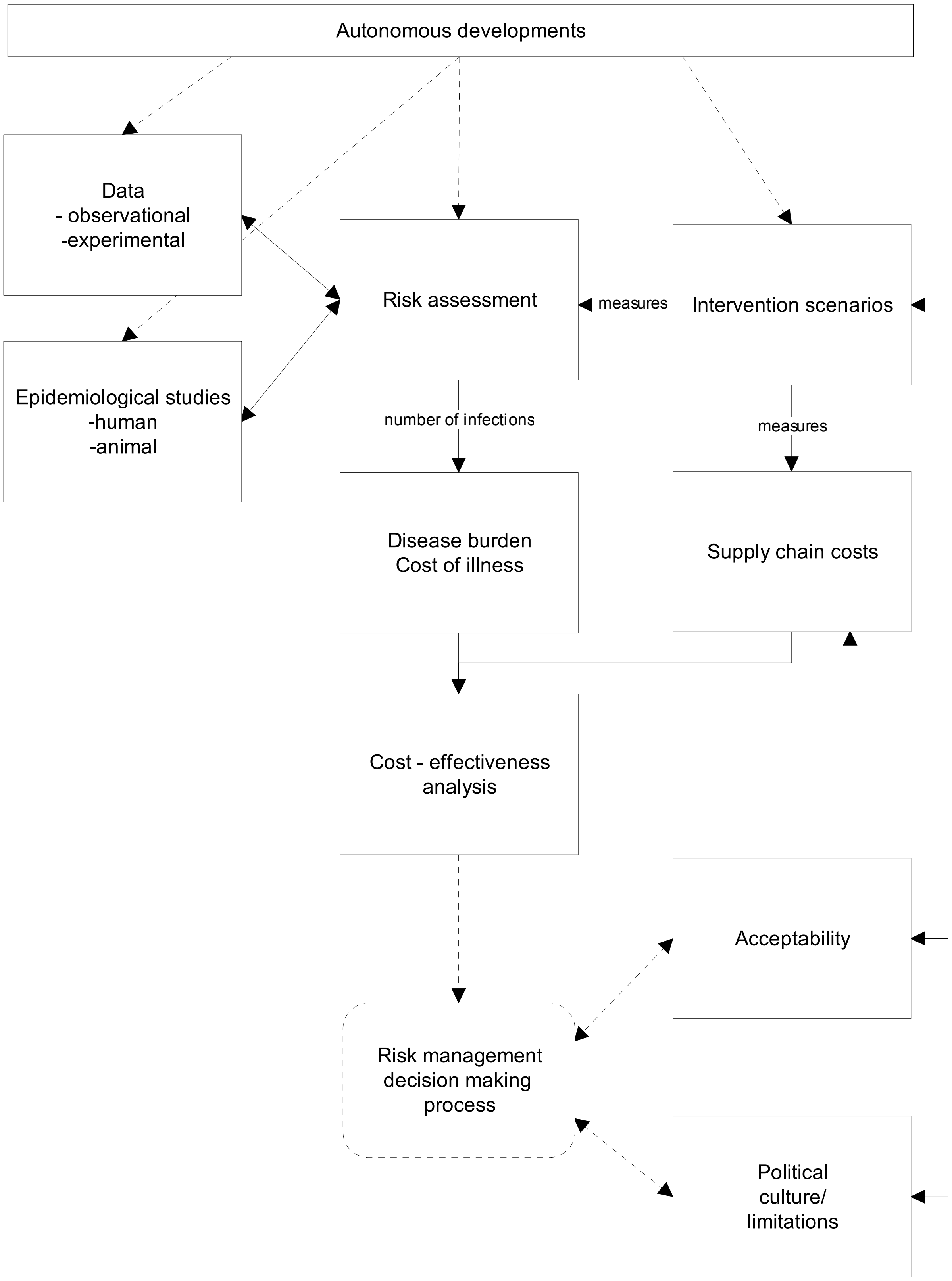


Figure 1. Design of the CARMA project.

1.3.1 Efficiency

Here, efficiency is defined as the degree to which an intervention achieves the desired results in relation to the efforts expended *in terms of money, time and resources* (Last, 1995). In other words, efficiency refers to the extent to which a goal can be achieved with fewer means, or the extent to which the same means can contribute to reaching a more ambitious goal. Efficiency deals with costs and benefits. An intervention measure is more efficient than any other measure when the former attains the same benefits at smaller costs, but also when the former attains higher benefits at the same costs. To evaluate efficiency, the possible effects of an intervention are estimated using a risk model, and are expressed as a reduction in the incidence of infections with *Campylobacter* spp. The results of the risk assessment model are fed into a model estimating the disease burden and cost of disease. The expected changes in disease burden and cost of disease, relative to a situation without intervention measures, are evaluated. Different decision criteria can be derived from the economic analysis. In the CARMA project, we will focus on:

- The (net cost per) absolute reduction in number of cases of illness or death;
- The absolute increase or decrease in production costs;
- The net costs per quality adjusted life year gained.

For each of these criteria, different interventions can be ranked on a scale from most to least efficient. Alternatively, interventions may be evaluated on the basis of a predetermined criterion, e.g. the net costs per quality adjusted life year should not exceed a certain threshold value. No such threshold values have yet been defined for food safety interventions. As an additional source of information, the results of the calculations will be compared with those of other interventions in preventive medicine, such as vaccination, environmental regulations etcetera. It is then up to the risk managers to decide which criteria will be used for decision-making, and in what manner.

1.3.2 Effectiveness

Effectiveness is defined as the extent to which an intervention, when deployed in the field in routine circumstances, does what it is intended to do (after Last, 1995). In other words, the extent to which an intervention contributes in achieving a certain goal. Effectiveness deals with the extent to which an intervention measure theoretically contributes to the reduction of the contamination of Campylobacter in chicken meat. It depends on the practical implementation of an intervention measure by the target group (farmers, slaughterhouses, processing plants, retailers, transport etcetera.). Practical implementation deals with: a) the extent to which an intervention measure is actually applied, e.g. a few processing plants do not implement the intervention measure at all; and b) the way in which a measure is being applied, e.g. a few processing plant do not implement the intervention measure correctly. Besides intended effects, an intervention can result in unintended, undesired effects.

If possible, the risk model to be developed should incorporate both intended and unintended effects of interventions. It is essential to mark the system borders as clear as possible: define which effects will be included and excluded from the analysis.

1.3.3 Legitimacy and acceptability

Legitimacy has to do with the extent to which an intervention, but also its effects, is supported or accepted by the society. This includes both the stakeholders in the chicken meat chain (e.g. farmers; processing plants) and the consumers as buyers of chicken meat products. Acceptability is associated with a positive attitude of stakeholders. It has to do with actual behavior, observing the measures opposed. Furthermore, legitimacy is associated with political acceptability, e.g. do the national government, other Ministries, members of the Parliament and the European Commission support the measure(s) to be taken? Within CARMA we will focus mainly on the societal acceptability, i.e. the extent to which stakeholders within the chicken meat chain and consumers accept an intervention measure. Political acceptability will not be a main focus of the CARMA project.

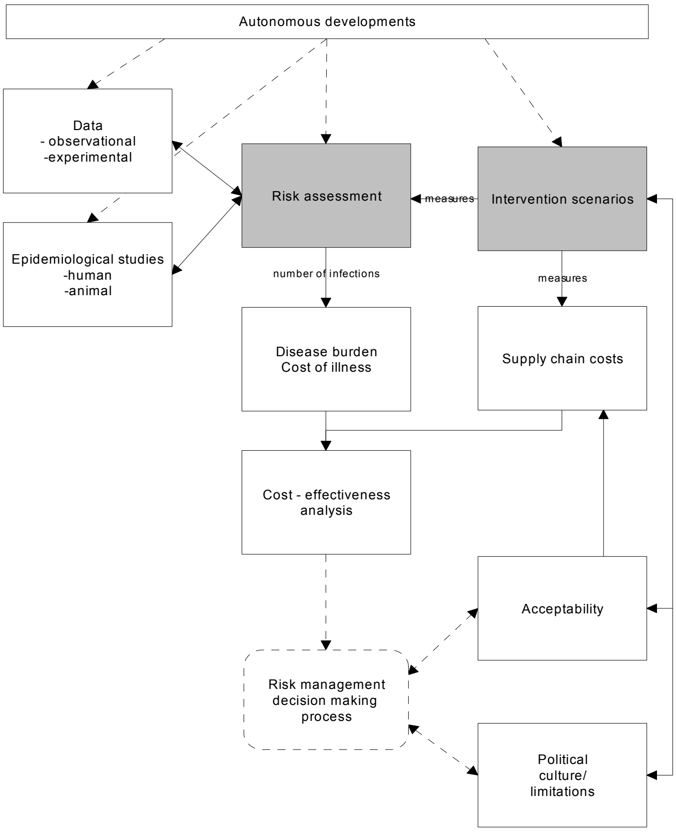
1.3.4 Risk Culture

Besides information about effectiveness, efficiency, societal acceptability and political support, the political culture plays an important role in decision-making. Political culture shapes risk managers' belief system about risk and risk management, as well as their choice of styles of interaction between government and business. According to Hoppe and Peterse (1993), the course and the end of a decision making process cannot be explained as a conflict of interests between different governmental bodies, but as a conflict between ideologies and cultures of the organisations involved. Culture sets the way in which one looks to a risk, and how to control that risk.

1.4 CARMA in progress

Current work focuses on the risk model for the consumption of chicken meat, describing the transmission of thermophilic *Campylobacter* spp. throughout the chicken meat chain, from the farm level to the consumer. This work will continue with combining the resulting consumer exposure estimates with dose-response models in order to estimate the annual number of cases of Campylobacteriosis in the starting situation (the year 2000). In addition, both the associated disease burden and economic losses will be assessed. A series of potential intervention measures has been selected, including interventions at the farm level as well as during processing, and at the consumer level. These interventions will be implemented in the models and their associated costs will be estimated. In the last phase of the project, a cost-effectiveness analysis will be carried out. A first series of analyses of political and societal factors affecting decision-making has been completed and further work will focus on the support for selected interventions. There appears to be a relationship with costs: intervention measures with a low level of stakeholder acceptance will require larger efforts, and thus higher costs, to be effectively implemented (Ogus, 1994). These issues will receive attention in the next stages of the CARMA project.

2. Modelling public health risks of *Campylobacter* spp. and the efficiency of interventions



2.1 Quantifying the contribution of different sources of contamination

As indicated in Chapter 1, there are many different potential routes by which humans can be contaminated with *Campylobacter* spp. and there is currently insufficient information to quantify the contribution of different sources. In the CARMA project, two approaches are being used to address this problem.

The first approach is based on estimation of theoretical exposure by different routes. It is assumed that the probability of infection or illness is proportional to the exposure to campylobacters per unit of time (e.g. year), and that the dose-response relation is similar for all transmission routes. To estimate the exposure via different routes (e.g. a food product), data are collected to estimate the amount of ingested food per eating occasion, the number of eating occasions per year and the concentration of campylobacters in ready-to-eat food. Similar calculations can be made for exposure to water (recreational or drinking-water) and possibly also for direct contact with animals. It is not possible to make these estimates for infections acquired abroad.

The second approach, which is carried out in a separate project (the Casa study), is the epidemiological approach through a case-control study. Using cases identified in medical microbiological laboratories, the relative importance of the different transmission routes can be determined. For factors that are significantly associated with the risk of campylobacteriosis, the population attributable fraction can be calculated. It is assumed that risk factors for acquiring severe illness (i.e. leading to consultation of a medical practitioner and submission of a faecal specimen for diagnosis) are similar as for cases in the general population.

Probably, neither of the above mentioned approaches will provide definitive information and it will be attempted to combine the information from these two methods to produce the 'best' estimate of the fraction of cases attributable to different sources. As the current focus of preventive regulations is on chicken meat, a specific attempt will be made to quantify the number of cases that can be attributed to this source. This result will serve as an anchor for the chicken meat risk model that will be used to estimate the effects of interventions in the chicken meat chain as well as the preparation of chicken meat in the kitchen.

2.2 The chicken meat risk model

Microbial risk models can be divided into two different stages: a) exposure models; and b) effect models (Figure 2). The exposure model quantifies the number of bacteria that are ingested by a (population of) consumer(s) per occasion of exposure (e.g. consumption of a meal) and the number of exposure occasions per time unit (e.g. a year). This information is fed into the effect model that aims to quantify the incidence of infections per time unit. The results of the effect model are an input to the economic analysis.

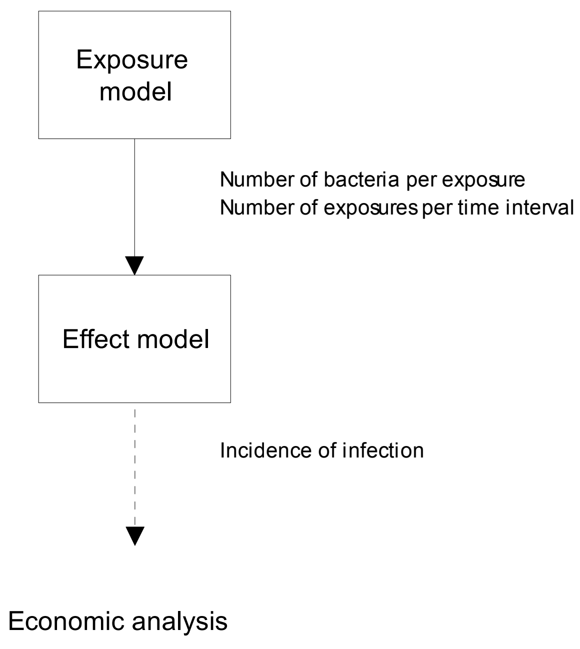


Figure 2. The relationship between exposure modelling and effect modelling.

Box 1. Accounting for variability and uncertainty

Microbial risk models explicitly account for variability in the system to be modelled and uncertainty about that system. *Variability* is usually defined as the inherent heterogeneity of a system, e.g. variation between the numbers of pathogens in different portions of food, variation in susceptibility of different consumers etc. Variability cannot be reduced by further measurements. Variability is described by some kind of probability distribution. Stochastic models such as Monte Carlo simulation models are then used to account for the effects of variability on the risk estimates. The major result of a risk model that includes variability is the expected (or long-term average) number of cases in the population. An additional possible output of a stochastic model is the degree of variation around this long-term average. If the variation is large, risk managers may decide to account for this in their decisions. Also, information on variation is important when comparing risk estimates to data from epidemiological surveillance. However, in the CARMA project we will focus on the average risk.

Uncertainty is usually defined as a lack of perfect knowledge about a factor in the model that represents the system. Further measurements or other efforts can reduce such uncertainty, but usually there remains considerable uncertainty that needs to be taken into account in the analysis. In the CARMA project, we will consider two types of uncertainty. *Parameter uncertainty* arises because of the limited number of measurements that are usually available to estimate the value of the parameters in the model. The uncertainty about a parameter can be described by some kind of probability distribution. To account for parameter uncertainty, a variability model as described above is simulated repeatedly, each time with a different set of possible combinations of parameter values. The main result of these calculations is a distribution of possible values of the average risk, representing the degree of confidence that we can have in the risk estimate. There are other kinds of uncertainty that usually receive less attention, but may be more important than parameter uncertainty. These include *scenario uncertainty* (descriptive errors, aggregation errors, errors in professional judgement, incomplete analysis etc.) and *model uncertainty* (uncertainty due to necessary simplification of real-world processes, mis-specification of the model structure, model misuse, use of inappropriate surrogate variables etc.). In other words: how well did the analyst process all available information and how well does the model represent reality? Such questions cannot be dealt with in Monte Carlo simulations but need a different approach. *Sensitivity analysis* is one tool to evaluate the effects of such uncertainty. How does the end-result change if other choices had been made? Alternative choices may be related to the use of one particular dataset to estimate parameter values, while many datasets are available, or to the use of one mathematical formula to represent some processes, while other formulas are possible as well. By quantifying the effects of realistic alternatives, based on a plausible rationale, an impression of the robustness of the model is obtained which is of great importance for the degree of confidence in model results and in decisions based on the model.

The degree to which variability and uncertainty can and should be included in a model depends on the availability and quality of data, and on their impact on the model results. A general choice cannot be made beforehand. In principle, the CARMA risk model will attempt to account for both uncertainty and variability. Several quantitative microbiological risk assessments on Campylobacter in broiler chickens have been performed so far (Christensen *et al*., 2001; Hartnett *et al*., 2001, Anonymous, 2002). To quantify exposure, process risk models were constructed, based on process knowledge and available microbiological data. The methodologies applied were somewhat different, but in each of them stochastic models were built, and Monte Carlo simulations were performed. The ‘Farm to Fork’ risk assessment methodology applied in these studies is being elaborated in the CARMA risk model for chicken meat to fit into the Modular Process Risk Modelling (MPRM) framework that is under development at RIVM (Nauta *et al*., 2001; Lindqvist *et al*., 2002; Nauta, 2002; Anonymous, 2003). Within this framework, a more mechanistic modelling of the basic microbial processes growth, inactivation, mixing, partitioning, removal and cross-contamination is applied. This has the advantage that model construction is less data dependent and more transparent.

The first objective of the chicken meat risk model is to describe the exposure of the Dutch population to thermophilic *Campylobacter* spp. as a consequence of the consumption of chicken meat. The consumers' exposure is derived from modelling the transmission of Campylobacter through the chicken meat chain, from farm until consumption (Figure 3). The complete chicken meat risk model will include transmission models for each stage of this chain, and will also account for the effects of imported meats.

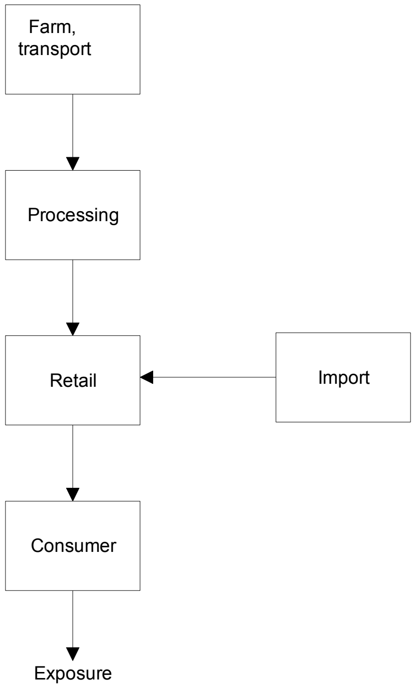


Figure 3. The chicken meat risk model assesses exposure by modelling the transmission of Campylobacter through the chicken meat chain.

The second objective of the risk model is to estimate the health risks associated with consumption of chicken meat. To this end, the results of the exposure module are fed into the effect module. A dose-response model estimates the probability of infection per exposure occasion in relation to the ingested dose. Subsequently, individual risks are aggregated over the whole Dutch population to produce an estimate of the number of Campylobacter infections per time interval (e.g. a year). The outcome of the dose-response model is fed into the economic model to estimate the associated disease burden and costs (see Chapter 4).

Development of the model will first concentrate on risk associated with chicken breasts, because the amount consumed is relatively high and because it is often handled raw in the kitchen (cutting, coating with breadcrumbs etc.) which involves risks for cross-contamination. In a later stage attention will also be given to other products (with skin) such as whole chickens and drumsticks, because the prevalence of Campylobacter in these products is usually higher than in chicken breasts.

Currently, more than 99% of all broilers are produced in intensive farming systems, where birds are typically held in large, closed stables where contact with the environment can be controlled to an important degree. There is however a trend towards organic production, which involves free access to the environment. Consumers value the animal welfare aspects of this type of production system and governmental policies support these developments. Therefore, the risks of organically produced chicken meat will be evaluated separately. In doing so, it is assumed that the major differences will be in the primary production, and that processing and later stages will be similar to those of conventionally produced broilers.

Processing of broilers is a highly standardised activity world-wide, and one generic model for the slaughtering process will be developed. Two types of products will be evaluated: pre-packaged, as typically supplied to supermarkets and unpacked, as typically sold by butchers, poulterers, on markets etc. Approximately 10% of birds slaughtered in the Netherlands are produced abroad, mainly in Belgium and Germany just over the Dutch border. Information on Campylobacter status of these flocks, such as provided by the Product Board for Meat, Poultry and Eggs includes these birds, so they will not be differentiated from birds broiled in the Netherlands. More than half of the Dutch chicken meat is exported (Havelaar, 2002), whereas a substantial proportion of the domestically consumed meat is imported from EU or non-EU countries. Precise information of how imported meat is further traded are scare. Therefore, when assuming that of the 285,000 tons imported poultry meat (PVE, 2001) in 2000 100% and 0%, respectively, would have been consumed in the Netherlands, 7-8% and 45%, respectively of the Dutch slaughtered and processed poultry meat would have been only consumed in the Netherlands. Within the CARMA project we therefore will search for new sources, in order to get better estimates.

In the CARMA project, we will focus on the risks for the Dutch population, i.e. the risks associated with consumption of domestic and imported chicken meat as marketed in the Netherlands. This choice implies that the true benefits of interventions in the Dutch chicken meat chain will be underestimated because health benefits will also be realised in countries that import Dutch chicken meat. To formally quantify such benefits, information on disease burden and cost of illness in importing countries would be necessary. This is beyond the scope of the current project. However, an attempt will be made to estimate the order of magnitude of benefits in other countries by accounting for exported volumes of chicken meat. This problem illustrates that ideally, cost-effectiveness analyses of interventions in the food supply chain should be undertaken at an international level.

2.3 Interventions in the chicken meat chain

The effects of interventions will be assessed in comparison to the state in the base year, 2000. This year has been chosen because it is relatively recent, there were no major food crises that have affected primary production and there is a relative abundance of data on both the chicken meat chain and on public health. Autonomous developments since 2000 will separately be taken into account. Many interventions may be considered to reduce the contamination of chicken meat with *Campylobacter* spp. The Steering Committee of the CARMA project, which includes risk managers at the Ministries of Public Health and Agriculture, have indicated priorities for interventions to be implemented in the risk model. After discussion with the Industry Forum[1] and experts in the field, the following intervention measures, concerning primary production, slaughtering and processing, consumer behaviour and imported meats have been selected for evaluation:

2.3.1 Interventions in primary production

The model for primary production developed for the CARMA project (Fischer, in preparation) indicates that the major risk factors for a Campylobacter positive flock are (i) infection

[1] The so-called ‘Industry Forum’ is composed of representatives of the Dutch chicken farmers, the Dutch slaughterhouses and processing plants, KvW, the two Ministries (Public Health and Agriculture), as well as the research institutes involved.

of the previous flock in the same house, (ii) presence of infected flocks in other houses at the same farm and (iii) other, unidentified factors. A recent UK report (ACMSF, 2003) stresses the importance of thinning[1] as a risk factor for contamination of broilers with Campylobacter. Thinning was also found to be independently associated with an increased risk of Campylobacter colonisation in a Dutch epidemiological investigation on 212 broiler farms (Jacobs-Reitsma *et al*., 2001). Data from the National Institute of Public Health and the Environment / the Inspectorate for Health Protection and Veterinary Public Health surveillance on zoonotic bacteria in farm animals have identified several risk factors for Campylobacter colonisation of broilers (Bouwknegt *et al*., 2003). A multivariate model indicated significant risks associated with the number of broiler houses on the farm, presence of other farm animals, hatchery, age of the broilers, season, region, and year. Univariate models also indicated effects of several hygiene associated factors such as ventilation system, presence of an anteroom, cleaning of boots, specific clothes and tools, type of drinking water and children entering the stable. A large proportion of the surveyed farms indicated that they already implemented the optimal hygienic measures. No data were obtained on the stringency of the application of these measures. Based on this information, the following interventions have been selected for evaluation:

1. Discontinuation of thinning. As the current market demand is mainly for chickens of around 42 days of age, we will evaluate the effect of lower stocking densities (35-38 kg/m^2 as compared to 42-45 kg/m^2). This will both obviate the need for thinning as well as result in increased animal welfare. This intervention will be compared with the actual situation with regard to stocking density and thinning in the base-year 2000.
2. Interrupt the transmission between successive flocks in the same house by increased cleaning and disinfection. For this purpose, the protocol developed to reduce *Salmonella* Java will be employed.
3. Monospecific farms, i.e. absence of other farm animals.

2.3.2 Interventions during slaughtering

There are many possibilities for reducing contamination during slaughtering, including:

1. Logistic slaughtering. Flocks that are tested negative for *Campylobacter* spp. will be slaughtered first, followed by flocks that are tested positive. Test results will be based on current bacteriological test procedures (samples being taken approximately 2 weeks before slaughtering) and rapid test that are currently being developed at ASG-Lelystad. Sampling for the rapid test procedures can be done at 1 day before slaughter. It is expected that this will significantly reduce the number of false-negative flocks[2].
2. Decontamination of the scald tank as a means of reducing cross-contamination by increased die-off of campylobacters in the scald water, in combination with stringent application of hygiene regulations and HACCP as it is acknowledged that currently, such procedures are not strictly enforced. True improvement of hygiene during slaughter may require development of new equipment and manufacturers will be approached for information.

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[1] Thinning means taking out at an earlier stage a part of the chicken birds from the flock for slaughter. The end weight of chicken birds namely determines the chicken birds density/m^2 at stocking. By thinning a flock, a higher chicken birds density/m^2 at stocking is possible.

[2] Odds ratio's for the occurrence of *Campylobacter* spp. in a broiler flock in relation to the age of the birds are: 22-28 days 1.00 (reference category); 29-35 days 2.34, 36-42 days 3.96 and > 42 days 3.02 (Bouwknegt *et al*., 2001).

3. Decontamination after slaughter. Several options will be studied:

   - freezing of chicken breasts, ready for distribution, 2 weeks at - 20 °C;
   - decontamination of whole carcasses by spraying and/or dipping with a 1-2% lactic acid solution and alternative disinfectants such as trisodiumphosphate;
   - dipping of whole carcasses in hot water;
   - irradiation or e-beam treatment of whole carcasses.

   Decontamination is not expected to reduce the prevalence of contaminated carcasses, but may reduce the number of campylobacters on a carcass. As the health risk is proportional to both the prevalence of contamination and the level of carcass contamination, such processes may result in considerable reductions of risk. However, the quality of the (fresh) product may be negatively affected.

4. Channelling. Meat from flocks that were known to be contaminated with *Campylobacter* spp. cannot be sold as fresh meat but may undergo heat treatment or other methods that reduce contamination to very low levels.

By combining these options, several interventions in the processing plants have been defined that will be evaluated in the risk model, based on enforcement of hygiene regulations as in the base year 2000 and with strict enforcement of HACCP (see table 1).

Table 1. Interventions in the processing plants to be evaluated in the CARMA risk model.

Logistic slaughter, test	**Decontamination**	**Channelling**
No	No	No
No	Yes	No
Conventional	No	Yes
Conventional	Positive flocks	No
Rapid	No	Yes
Rapid	Positive flocks	No

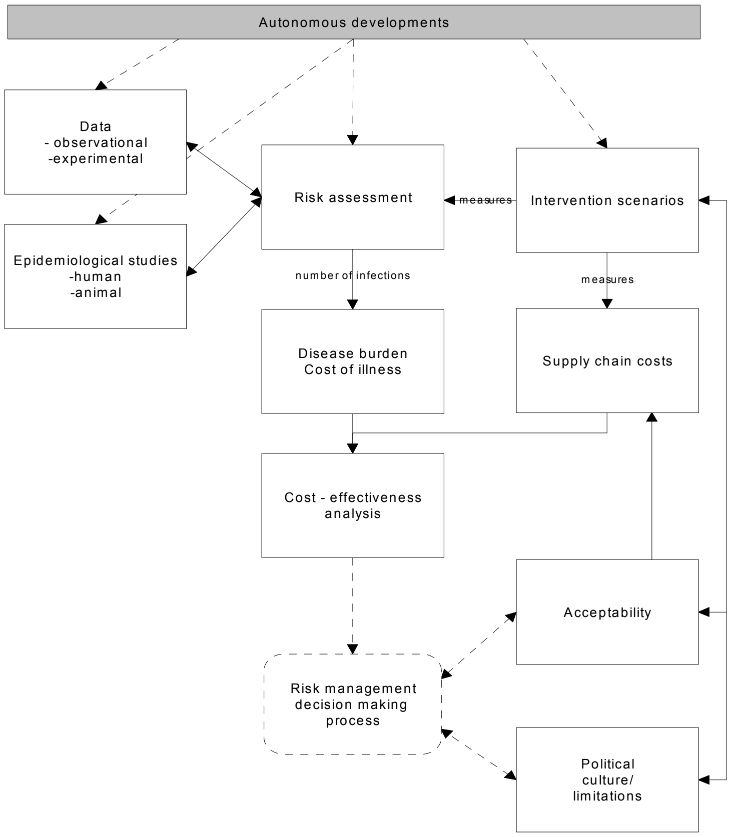
2.3.3 Influencing consumer behaviour

Proper (hygienic) handling and cooking chicken meat at home can also reduce human infections with Campylobacter. Labelling and education are suggested measures that can influence handling and cooking. Information or advice to consumers can be given in several ways: information campaigns (television, radio, handouts, Internet etcetera.), advertisements, education on schools and universities, courses etc. Little is known about the effectiveness of education and labelling on sustained improvements of hygiene behaviour by consumers. Therefore, these intervention measures will be included by formulating and verifying assumptions. Experts in social sciences will be asked to estimate the degree to which education might affect critical parameters in the consumer phase model. Furthermore the home freezing of chicken breasts will be evaluated. It is expected that some consumers routinely stores the product in the deep-freezer for some days to a week, and the option of promoting this practice will be evaluated.

2.3.4 Testing of imported meats by government

A large proportion of domestically consumed chicken meat is imported from other EU countries or worldwide. If the level of contamination with *Campylobacter* spp. is high, measures in the Dutch production system may have a limited effect on public health within the Netherlands. It is therefore important to know the quality of imported meats in comparison to Dutch products. Even though meat produced in the EU cannot be banned from the Dutch market, sensitivity analysis can be applied to evaluate the effects of reduced contamination of such products.

3. Autonomous developments



3.1.1 Chicken meat producers

Since 1985 the number of chicken producers in the Netherlands has decreased. In 1985 1,459 chicken producers were responsible for the production of more than 38 million chickens. In 2001 that number had increased to 50,1 million chickens held by 1,027 companies. In this period, the average number of birds per farm almost doubled from 28,000 to 49,000 birds. This implies that there is a movement towards concentration and an increase in average farm size. A particularity is the so-called 'fertiliser quotas' in the Netherlands, limiting the Dutch chicken farmers in their expansion (Berkum *et al*., 2002). Most of the chickens produced in the Netherlands are also processed here, with a large number of Dutch chickens being produced under contract[1]. In more recent years, Dutch chicken meat producers have had to compete strongly with low costs production countries, such as Brazil and Thailand (Tacken *et al*., 2003; PVE, 2003). Apart from low costs production countries outside the EU, the ongoing expansion in the chicken meat production within the EU resulted in a decrease of the producer market price in 2002 (PVE, 2003). However, the costs of interventions have to be covered by producers' returns. This return is largely determined by the market price of chicken meat. This holds for both the conventional and the 'ecological' produced chicken.

The Dutch 'ecological' chicken production is very small scale. According to Stichting Natuur en Milieu (2001), less than 0.1 % of Dutch chicken meat is classified as 'ecological'. The dif-

[1] Different type of contracts exists, but in all cases the purchase of the chicken birds by a slaughterhouse is regulated before purchasing the 1-day old chickens.

ference in cost price between 'ecological' and conventional produced chicken meat is largely a result of high prices of 'ecological' feed for chicken. Furthermore a large part of the Dutch demand for ecological chicken meat is met by imported French chicken, produced at lower cost (Berkhout *et al*., 2003). The risk that products of 'ecological' and free-range held chickens contain Campylobacter or Salmonella bacteria is probably greater than for products of conventionally reared chicken (Swarte *et al*, 2002: 13-14). Nevertheless, the Dutch government is striving for a market share of ecological food products (fruit, vegetables, dairy, bread, meat) of up to 5% in the Netherlands in 2004 and up to 10% in 2010. In 2002 the market share amounts to 1.6% (Platform Biologica, 2003)

3.1.2 Slaughtering, processing, and import and export streams

Concentration in the chicken meat production chain also involved slaughterhouses and processing plants. From the 91 slaughterhouses in 1985, only 34 slaughterhouses were still in operation in 2001. The annual supply to the large slaughterhouses increased, whereas the supply to small slaughterhouses decreased. Around 10-20 % of the slaughtered birds are from outside the Netherlands. However, Dutch processing plants do process imported chicken meat, e.g. lightly salted or frozen chicken meat from Brazil and Thailand (Tacken *et al*, 2003). Approximately 35-45% of the chickens slaughtered in the Netherlands go to the meat processing industry for further processing, such as ready to eat meals and snacks. The remaining part of the fresh chicken meat is bought by retailers (for at-home consumption, approximately 45-50 %) and by restaurants, hotels and caterers (approximately 10-15 %) (Tacken *et al*., 2003).

More than half of fresh chicken meat and chicken meat products processed in the Netherlands is exported. The slaughterhouses/processing industry sell their products particularly to other EU countries (approximately two thirds of the export market), Eastern Europe (nearly 10%) and a quarter goes to other countries around the world. Within the EU, Germany and the United Kingdom are the main markets for Dutch chicken meat.

In order to be able to compete on the poultry world market, the around 300 processing plants in the Netherlands use several strategies. Besides improving quality, aiming at innovative products or improving the efficiency of the chicken meat chain (integration), scale enlargement is another strategy (Agrarisch Dagblad, 2002b). High labour costs and heavy requirements in the field of animal welfare, environment and food safety lead to higher costs of production of chicken meat in the Netherlands in comparison with countries like Brazil and Thailand. Due to these higher production costs, chicken meat producers in the Netherlands find it hard to compete on the world market where customers are focusing on the cost price of chicken meat. In order to have prospects, poultry farming and industry in the Netherlands needs to change. The triangle Paris – London – Berlin with its around 150 million consumers is a very good market for Dutch food industry. In the future the opportunities for the Dutch poultry farming and industry are in optimal service of the fresh product market in North-West Europe. This means guaranteeing food safety, full transparency of the food production chain, constant product development and innovation, anticipating on 'ready to (h)eat' products, and new production methods and concepts concerning social accountability (Wageningen UR, 2003).

The possibilities for export of Dutch chicken meat can also be influenced by government policies of importing countries. For example, the Russian government has decided recently to increase its own chicken meat production by 80% in the years to come. Consequently, Russia will have to import less chicken meat in the future, assuming that consumption in Russia stays more or less constant (LNV, 2003).

3.1.3 Food retail

In 2000, Dutch consumer expenditure on meat, including chicken meat and meat products, amounted to approximately € 4.5 billion (including VAT). That is on average € 280 per head of the population. Poultry (in particular chicken) contributes 12% of the total expenditure on meat. About two thirds of this consumer expenditure took place in supermarkets. In 2001, the supermarkets market share, the butchers share and the poulterers share amounted to 73%, 18% and nearly 10%, respectively (Hoofdbedrijfschap Detailhandel, 2002). Given that the number of butchers is still decreasing, the market share of supermarkets will probably increase further (in 2002 already 80.6%). Especially small butchers with few or no personnel have had to close their business because they cannot compete anymore with the supermarkets. The market share of supermarkets for fresh meat is increasing by 1 percentage point every year, particularly for prepacked meat, meat products and chicken. This is stimulated by improved packaging methods causing improved storage life of products (ING bank, 2000). Large quantities, resulting in special offers, and the convenience of one-stop-shopping, attracts the consumers to buy prepacked meat at the supermarket rather than from a butcher or poulterer (Bedrijfschap Slagersbedrijf, 2001).

Within the next five years, large supermarkets intend to sell meat produced by slow-growing chickens (Silvis *et al*., 2000). Finishing chickens in 56 days in stead of the 42 days needed at present is expected to improve the well being and the health of the chickens. However, the production costs will increase, as will the period during which contamination with Campylobacter is possible. Meat of these slow-growing chickens will be sold as ‘welfare’ meat at higher prices (Agrarisch Dagblad, 2002a).

3.1.4 Away-from-home and at-home consumption

In 2002, consumption of chicken meat in the Netherlands increased by 0.3 kg up to 22.4 kg (table 2). This includes both consumption at home and consumption away from home (hotels, restaurants, canteens etc.). However, only half of the purchased chicken meat is finally consumed, the other half is bones and other waste left on the plate (PVE, 2002). In 2001, total Dutch consumer expenditure on chicken meat amounted to € 660 million (incl. VAT).

Table 2. The Dutch consumption of chicken meat in kg/head, 1990 – 2002 (Source: PVE, 2002).

	1990	1995	1999	2000	2001	2002
Total consumption of poultry meat (kg/head)	17.3	20.4	21.4	21.6	22.1	22.4
- Chicken (kg/head)	12.9	15.2	16.2	16.7	17.1	17.2
- Turkey (kg/head)	1.8	2.7	2.6	2.2	2.3	2.5
- Other (kg/head)	2.6	2.5	2.6	2.7	2.7	2.7

The retail sector sells mainly chicken meat products for preparation and consumption at home, with a raising supply of ready-to-eat meals in recent years (Bedrijfschap Horeca en Catering, 2003). Ready-to-eat meals count for almost 12% of the total volume of consumer buying. Long storability, shelf-life and the ease of deep-freezing food products (as full alternative for dinner) are attractive attributes for the consumer. Ready-to-eat meals, meat snacks and meat substitutes are mostly bought in the supermarket. More exclusive (and more expensive) products like beef, veal and lamb are still mostly purchased at special stores. Furthermore, the contribution of pre-packaged meat and meat products has increased from

42% in 1990 up to 76% in 2001. Supermarkets opposite to the other retail segments, are mainly selling pre-packaged meat and meat products in self-service area (ING bank, 2000).

Besides through consumption of chicken meat at home, consumers may acquire Campylobacter infection through away-from-home consumption. Less time for cooking at home and an increase in spending power have stimulated the increase of away-from-home consumption. Away-from-home consumption of chicken meat takes place both in traditional ‘horeca’ establishments such as (fast-food) restaurants and hotels, and through catering facilities such as hospitals and company restaurants. The strong growth of fast-food restaurants has stimulated the growth of market share of poultry meat in the total away-from-home expenditure on meat. In the period 1991-2000, this market share has increased from 26.9 % to 32.2 % (Voorlichtingsbureau Vlees, 2000). As with consumption at home, chicken breast dominates consumption in the away-from-home market (see table 3).

Table 3. Away-from-home consumption of different kind of poultry meat, 1991-2000 (Source: PVE/GfK, CBS. Processed LEI).

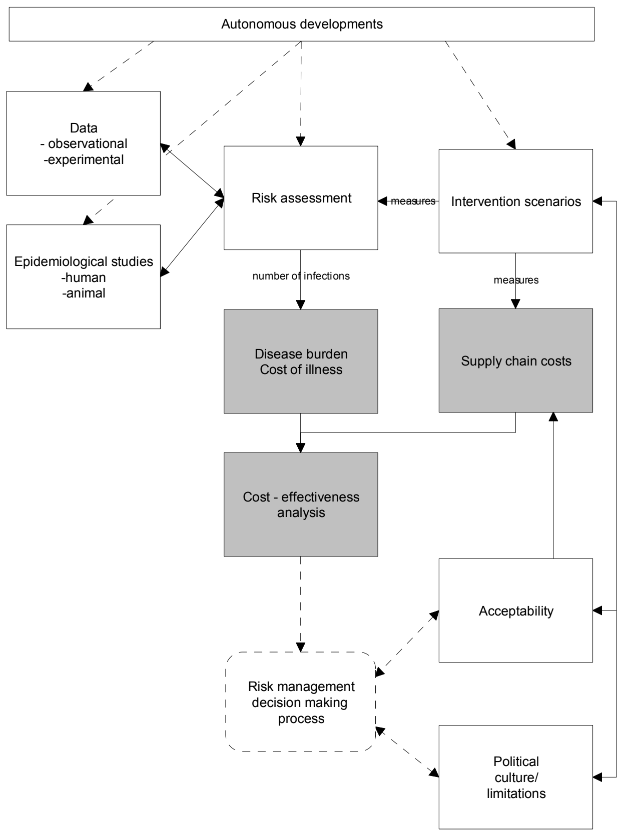
	1991	1994	1997	2000
Total (in tons)	26,057	30,545	37,071	40,786
- Chicken, whole/half	8,697	6,522	8,236	7,186
- Chicken, breast	6,769	8,332	11,015	14,425
- Chicken, leg	3,406	4,011	4,262	4,326
- Chicken, ready-to-cook/snacks	1,599	6,704	8,816	10,613
- Turkey	1,809	2,522	2,719	2,691
- Other	3,779	2,454	2,023	1,545
Population in the Netherlands	15,010,445	15,341,553	15,654,192	15,987,075
Away-from-home consumption of poultry meat (in kg/head)	1.7	2.0	2.4	2.6

The Council for the Rural Area (Raad voor het Landelijk Gebied, 1998) expects that the relationship between expenditures on away-from-home and at-home consumption will slowly move from 30-70 at present, to probably 50-50 in the future. Traditional consumption patterns will more and more disappear, and by that, forms in which food is being presented change. For instance, the volume of cut and pre-treated vegetables is rapidly increasing.

3.1.5 Incidents

Food incidents in the livestock industry have consequences for the poultry meat industry. In several EU member states, the BSE crisis of October 2000 has caused a decrease in the consumption of beef and an increase in the demand for poultry meat in 2001. The recent dioxin affair in Belgium and the Netherlands, whereby feed for chickens was contaminated with dioxin, hampered the export of poultry and poultry meat (PVE, 2003). But according to different studies, neither the BSE crises nor the foot-and-mouth disease crisis (in March 2001) had a negative influence on the image of meat. In 2001, consumers regarded chicken meat as having more quality, being more suitable for many dishes, healthier and more environmental friendly produced than the year before (Voorlichtingsbureau Vlees, 2002).

4. Economic analysis



4.1 General introduction

Within the CARMA project, the disease burden model, the cost of illness study, the study of the costs of interventions for the chicken meat supply chain and the cost-effectiveness analysis all aim at providing information on the relative efficiency of several interventions to prevent Campylobacter infections in the population. The output of the risk assessment model, in terms of number of expected Campylobacter infections per age group per period, will serve as input to the disease burden model, that estimates the burden of disease and corresponding cost of illness (see figure 1). Separately, costs of the interventions under study for all stakeholders in the chicken meat chain will be estimated. For all preventive interventions to be modelled in the CARMA study, the costs of the intervention in the chicken meat chain will be related to (reduced) burden of disease and (reduced) cost of illness. This results in a cost-effectiveness ratio (CER), expressing the relative efficiency of several policy options to reduce the number of Campylobacter infections.

4.2 A framework for economic analysis

The objective of the CARMA project is to analyze different intervention strategies that might result in a reduction of the number of human Campylobacteriosis in the Netherlands. Given this objective, the economic setting should then allow us to judge the success of the interventions, in terms of its impact on health status (Belli *et al*., 2001). Several forms of economic evaluation of health programs are available. Drummond *et al*. (1997) provide a framework for such analyses. Four major types of full economic evaluation studies (as opposed to partial economic evaluation) are available: cost-minimisation analysis, cost-effectiveness analysis, cost-utility analysis and cost-benefit analysis. With a cost-minimisation analysis, equal effectiveness of all programs under review is required, and the cheapest program is thus considered the most attractive. This type of analysis is e.g. useful in the comparison of two alternative drugs that have the same effect. In the current project, it is expected that different strategies to reduce human campylobacteriosis have different effects, e.g. in terms of the number of human cases of Campylobacter infections averted, so cost-minimisation analysis would not be the best research design. A less used form of economic evaluation research in human health economics is cost-benefit analysis, although it is considered as the 'gold standard' in other economic fields. Its aim is to express all costs and all effects in monetary terms. One of the major problems in this type of research is the valuation of effects. What is the monetary value of an improvement in quality or length of life? Within CARMA, these problems will not be addressed and therefore, cost-benefit analysis is not the research design of choice. Cost-effectiveness analysis (CEA) is a form of full economic evaluation, where both costs and health consequences of alternatives strategies are examined. In cost-effectiveness analysis, costs are related to a single, common effect that may differ in magnitude between the alternative programs (Drummond *et al*., 1997). The results of such comparisons may be stated either in terms of cost per unit of effect, or in terms of effects per unit of cost. In the case of a cost-effectiveness analysis of interventions directed at the reduction of Campylobacter infections in humans, the effect measure might be the number of cases of human campylobacteriosis averted. A special form of CEA is cost-utility analysis (CUA). Here, the aim is to link net cost of an intervention to the combined effects of the intervention on mortality and morbidity. Within the CARMA project, the economic evaluation of interventions to reduce campylobacteriosis will be performed both as a cost-effectiveness and as a cost-utility analysis. Further information on cost-effectiveness-analysis and cost-utility analysis will be provided in paragraph 4.5.

4.3 Estimation of disease burden and cost of illness

4.3.1 Disease burden

The economic analysis will start with the estimation of the disease burden and cost of illness of human campylobacteriosis in the Netherlands. These estimates will elaborate on a previous estimate of Havelaar *et al*. (2000), who estimated that human campylobacteriosis was associated with an annual loss of 1400 DALYs (90 % CI 900-2000) in the Netherlands. DALY is one of several metric methods to measure burden of disease, and represents both morbidity and mortality due to a certain health problem. Using the DALY metric, the burden of disease can be made comparable across diseases and possible interventions. The number of DALYs associated with a disease is the sum of the number of Years of Life Lost (YLL) and Years lived with Disability (YLD) in a certain year. To calculate YLL, the number of deaths and age at moment of death is needed. The remaining life expectancy at the time of death is calculated per sex from survival tables and aggregated over all deceased patients from the disease under study. To calculate the number of YLD, the average number of incident or prevalent patients (depending on the type of disease) is multiplied by a weight for the severity of disease. This weight is (close to) 0 for non-severe conditions, and (close to) 1 for extremely severe conditions. Further details are given in paragraph 4.5.3.

Since the estimate of 1400 DALYs related to Campylobacteriosis and sequelae was made by (Havelaar *et al*., 2000), new epidemiological data on the incidence of gastroenteritis due to Campylobacter became available. Therefore, an update of the previous estimate will be made in the context of the CARMA project. Besides, the DALY estimate will be extended with an estimate of the cost of illness due to human campylobacteriosis. To integrate these two estimates, which to a certain extent are connected to each other, a new model will be built. This model will describe the chances that certain groups of infected people will develop sequelae of infection, such as gastroenteritis, reactive arthritis, inflammatory bowel disease (IBD) and Guillain-Barré Syndrome (GBS). The model will distinguish between different degrees of severity for those sequelae. In the description of infected persons, the model will distinguish groups that differ with regard to age and sex.

The principle output parameter of the disease burden estimate will be the number of DALYs associated with Campylobacter infection. However, all intermediate endpoints, such as number of gastro-enteritis infections, number of severe sequelae and number of deaths will also be presented, at the level of the entire Dutch population.

4.3.2 Cost of illness

Table 4 provides a framework for costs that in principle should be included in a cost of illness study within a health economic context. Within the CARMA project, the reduction of the health problem under study of course has important (economic) implications in the chicken meat chain. These aspects will be discussed in paragraph 4.4.
The cost of illness study within the CARMA study will at least cover direct costs in and outside the healthcare system, and indirect costs outside the healthcare system (productivity losses). Following the Dutch guidelines on cost-of-illness studies (Oostenbrink *et al*., 1997), indirect costs within the healthcare system should be ignored. To be in accordance with the Dutch guidelines, as well as for ethical reasons, we too will not consider these costs within the CARMA cost of illness study.

Also, because of the difficulties in monetary valuation of intangible costs and lack of empirical data, they are ignored in the cost of illness study. However, they form part of DALY calculations as far as patients' reduced quality of life is concerned. So far, methodology to incorporate intangible costs related to suffering of relatives of the patient is lacking. Hence, these costs will be excluded from the analysis.

For each of the different health states associated with Campylobacter infection or its sequelae, cost estimations are needed for the cost of illness study. For gastro-enteritis, such estimations are available from the SENSOR study (Van den Brandhof *et al*., 2003). For reactive arthritis, IBD and GBS, cost estimates for the Netherlands are not available at present. It will be attempted to estimate the costs using data from hospitals, registries and literature.

Table 4. General outline of costs to be included in a health economic study of cost of illness of campylobacteriosis.

	Within health care system	Outside health care system
Direct Costs	**Acute gastro-enteritis**: General practitioner contacts Laboratory diagnostics Drugs Hospitalisations Other diagnostics Specialist care **Complications acute gastro-enteritis (Guillain-Barré Syndrome, reactive arthritis, inflammatory bowel disease):** General practitioner contacts Laboratory diagnostics Drugs Hospitalisations Other diagnostics Therapy Specialist care Revalidation Home care **Costs of epidemiological research / outbreak-surveys**	**Patient / family costs:** Travel costs patient Informal care by family members or third person Co-payments by patients, e.g. for use of alternative medicine
Indirect costs	Medical costs in life years gained (averted deaths), as a consequence of prevention of acute gastro-enteritis and its complications	**Productivity costs related to**: Days lost paid work by patients/ third person taking care of a sick person Days lost unpaid work by patients/ third person taking care of a sick person Days lost school Inability to work permanently Untimely death
Intangible costs	Reduced quality of life of patients following disease, pain, suffering, fear, etc. Reduced quality of life of family members of patients, following fear and distress related to the patient's disease	

4.4 Estimation of costs in the chicken meat chain, including costs of interventions

4.4.1 Estimation of industry costs

A preliminary estimate, based on Dutch data and extrapolation of international data, suggests that chicken is responsible for 40%, at the most, of all human campylobacteriosis (Havelaar *et al*., 2002). Therefore, the first step within the CARMA project is the analysis of various intervention measures to reduce *Campylobacter* in the chicken meat chain. A full description of the various intervention measures under study can be found in paragraph 2.3.

These various intervention measures are applied on different levels within the chicken meat chain. These levels are:

- The chicken producers, including all levels from the pedigree (élite) flocks until the commercial broiler chick flock;
- The transport industry;
- The slaughter and processing industry;
- The wholesalers and retailers;
- And the final consumer.

In most cases, the affected level is also the primary affected stakeholder who has to invest the additional industry costs triggered by the intervention measure taken. In the case of the final consumer however, public funds or chicken meat chain funds might have to be raised to pay for e.g. educational measures to teach the final consumer 'safer' food handling.

Given our priorities, we will therefore estimate the costs that are related to the various intervention measures under study. A list of the costs that might arise for the chicken meat chain by the application of the intervention measures under study is summarised in table 5. Some of these intervention measures might require only a single, but expensive investment, e.g. capital investments in a slaughterhouse. Capital investments are by definition long-lasting assets, which involve high financial costs. These costs remain unchanged in total for a given time period despite possible changes in the related level of total activity or volume (Horngren *et al*., 2000). Once a long-lasting asset is purchased or constructed, it is often difficult or costly to change, alter, or reverse a capital investment decision (Kay and Edwards, 1994). These investment costs will be depreciated following standard accounting principles. For other intervention measures, costs recur with each application (e.g. soap and disinfection materials, when cleaning and disinfecting a stable before repopulating with the following flock). These latter costs change mostly in relation to the total applied volume or activity (Horngren *et al*., 2000). Consequently, not all costs will occur at the same time, and also 'benefits' might be realised at different moments in the future. In order to be able to compare the different intervention measures under study, we will calculate the net present value for each of them and then compare average annual costs and benefits of the different intervention measures. Present values are calculated by discounting a future value back to the present, in order to find the current or present value (Kay and Edwards, 1994), as illustrated in figure 4. In this study a discounting rate of 4% will be used, according to the Dutch recommendation for public sector investments (Oostenbrink *et al*., 2000).

Table 5. General outline of costs to be included in an economic evaluation on intervention measures to reduce Campylobacter *in the chicken meat chain.*

Cost category	Affected
Industry costs[1)]	
Direct costs related to animal production [2)]	Increased (reduced) morbidity and mortality of animals on farms
	Reduced (increased) growth rate/feed efficiency and increased time to market
	Reduced number of cycles per year (additional time to disinfect stable between two flocks)
	Reduced number of chicken birds per cycle (no thinning out)
	Costs of disposal of contaminated animals on farm and at slaughterhouse
	Increased meat product spoilage due to pathogen contamination
Direct costs related to control costs for pathogens at all links in the food chain [2)]	Altered and new farm practices (bio-security measures, disinfection/sterilisation, sterilised feed, etc)
	Altered animal transport patterns (logistic transport, feeding/watering, disinfection/sterilisation, etc)
	New slaughterhouse procedures (logistic slaughtering, hide wash, knife sterilisation, carcass sterilising, etc)
	New processing procedures (pathogen test, logistic processing, decontamination, products development, altered shelf-life of products, etc)
	Altered product transport (e.g. increased use of time/temperature indicators)
	New wholesale/retail practices (pathogen tests, employee training, procedures, altered shelf-life of products, etc)
Direct costs related to outbreaks[3)]	Herd slaughter/product recall
	Plant closures and disinfection
	Regulatory fines
	Product liability suits from consumers and other firms
	Reduced product demand because of outbreak
	Increased advertising or consumer assurances following outbreak
Regulatory and public costs for controlling Campylobacter [4)]	
Disease surveillance costs to:	Monitoring pathogen incidence in the food chain
	Developing integrated database from farm to table for *Campylobacter*
	Developing cheaper and faster pathogen tests

[1)] A more complete list of industry costs can be found in Buzby *et al*. (1996). Within this table we will consider only costs that are appropriated for the intervention measures under study.
[2)] But apart of direct 'costs' related to intervention measures to reduce Campylobacter in the chicken meat chain, there might be also indirect 'benefits', such as: better control of other foodborne pathogens; better management systems and control of whole production process; etc. However, these later benefits are hard to quantify and are therefore in first instance not considered in the CARMA project.
[3)] According to Buzby *et al*. (1996) "direct costs related to an outbreak" are also a part of societal costs of foodborne illness. However, most human *Campylobacter* infections that are related to chicken meat, are sporadic cases. Therefore, in the first instance we will not consider them in our economic evaluation.
[4)] According to Buzby *et al*. (1996) regulatory and public health chain costs is another cost category of the societal costs of foodborne illness. However, some of these costs falls in the category of "public health" costs and are therefore considered in the cost-of-illness study (see table 4). Whereas the other public costs are more closely related to the chain itself and might have to be even financed by the chain itself. Within this list we will consider only the latter one. A more complete list on regulatory and public health chain costs can be found in Buzby *et al*. (1996).

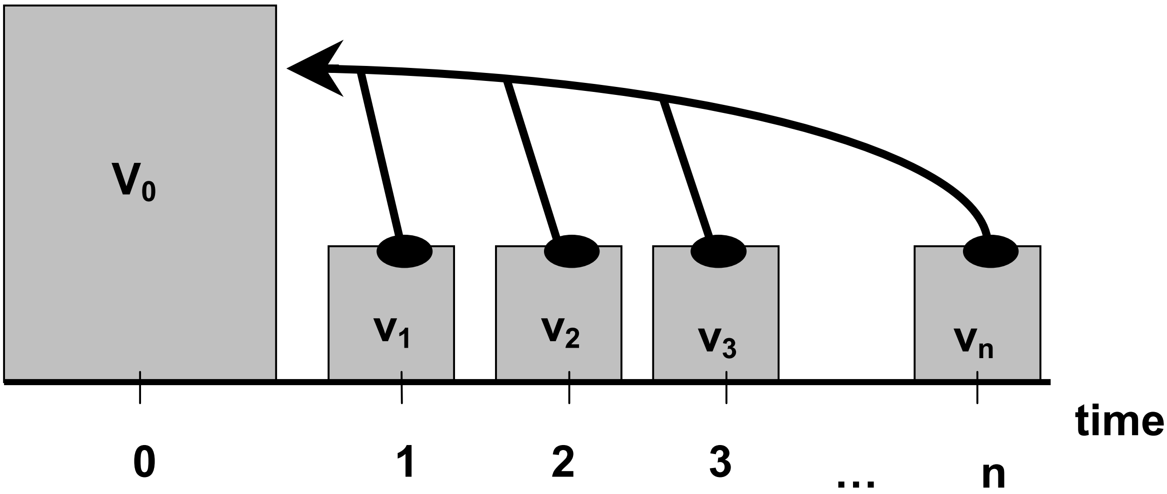


Figure 4. Illustrating the calculation of the net present value (V_0). Future values (v_i) occurring at time i (i = 1-n) are discounted one by one, and added together towards the net present value (Source: Däumler, 1983).

For all preventive interventions to be modelled in the CARMA study, the costs of the intervention in the chicken meat chain to control *Campylobacter* will be related to 'reduced' burden of disease and 'reduced' cost of illness. This will result in a cost-effectiveness ratio (CER), expressing the relative efficiency of several policy options to reduce the number of *Campylobacter* infections.

4.4.2 Necessary assumptions

In our cost-effectiveness analysis we will make the assumption that the Dutch chicken meat supply as well as the Dutch demand for Dutch chicken meat will be equal to that of the year 2000, our base year. This is an oversimplification and it assumes that none of the intervention measures under study would affect a) the Dutch supply of chicken meat and b) the Dutch domestic consumer demand of chicken meat.

In reality, however, the chicken meat chain is strongly vertically integrated and there is also high competitiveness between countries in this sector (Bondt and Van Horne, 2002). Most of the intervention measures under study however, will involve additional costs without a direct benefit for the investor. In order to survive, Dutch chicken meat producers and Dutch processing plants specialised in chicken might be forced to spill their additional production costs through to the final consumer. A higher product price for Dutch chicken meat, however, might have different effects on consumer demand and as such on the long-term supply of Dutch chicken and chicken meat. These possible effects are in summary:

- Given that the intervention measures applied in the Netherlands results in increased prices of Dutch chicken meat, Dutch and non-Dutch consumers might switch to non-Dutch, less safe, but cheaper chicken meat.
- Consumers might switch to non-chicken meat products, resulting in a spill-over to other meat (and probably also fish) markets. According to the findings of Mangen and Burrell (2001), chicken meat demand in the Netherlands is insensitive to price changes. Therefore, we might assume that in the Netherlands a slight rise in the consumer price for chicken meat, due to higher production costs, might not result in a demand change for chicken meat. However, in how far this holds for non-Dutch consumers is questionable.

- Despite the higher product price, health concerns may stimulate Dutch and/or European consumers to buy more expensive Dutch chicken meat. A temporary increase in the demand for Dutch chicken meat might be the consequence. This assumes however, that the Dutch chicken meat chain is the only one that has tackled the problem; that both Dutch and European consumers are well informed; and that other countries will take time before reaching a similar chicken health status as the Netherlands.
- Independent of the price for chicken meat and independently of all efforts taken to control *Campylobacter* in the chicken meat chain, consumers might switch to other meats due to health concerns.

Given the uncertainty of Dutch chicken meat supply and of Dutch demand for Dutch chicken meat, sensitivity analysis around these two factors will form part of our economic analysis.

4.5 Cost-effectiveness analysis

4.5.1 Unit of measurement

As stated in paragraph 4.2, the economic evaluation of interventions to reduce human campylobacteriosis will be in the form of both cost-effectiveness analysis (CEA) and cost-utility analysis (CUA). Although aa variety of output measures may be chosen as a reference in CEA, the cost per case (i.e. infection) averted and the cost per life year gained are most commonly measured. Both measures of cost-effectiveness will be reported in CARMA.

In cost-utility analysis, two metrics that may be used as an indicator of outcome are quality adjusted life years (QALYs) and Disability Adjusted Life Years (DALYs). These metrics both quantify morbidity or/and mortality outcomes and make them comparable across diseases and possible interventions. While QALYs aggregate the actual health quality over time, DALYs aggregate the loss of health compared to perfect health. DALYs and QALYs complement each other during a typical course of life, as is demonstrated in figure 5. DALYs are the black part of the rectangle. QALYs are the grey part of the rectangle. The measures do not overlap, but are complementary parts. The black valleys represent acute disease episodes over one's lifetime. The black space at the far right indicates premature death. The downward tapering of the grey QALY area indicates chronic disease that is continuous until the early end of life.

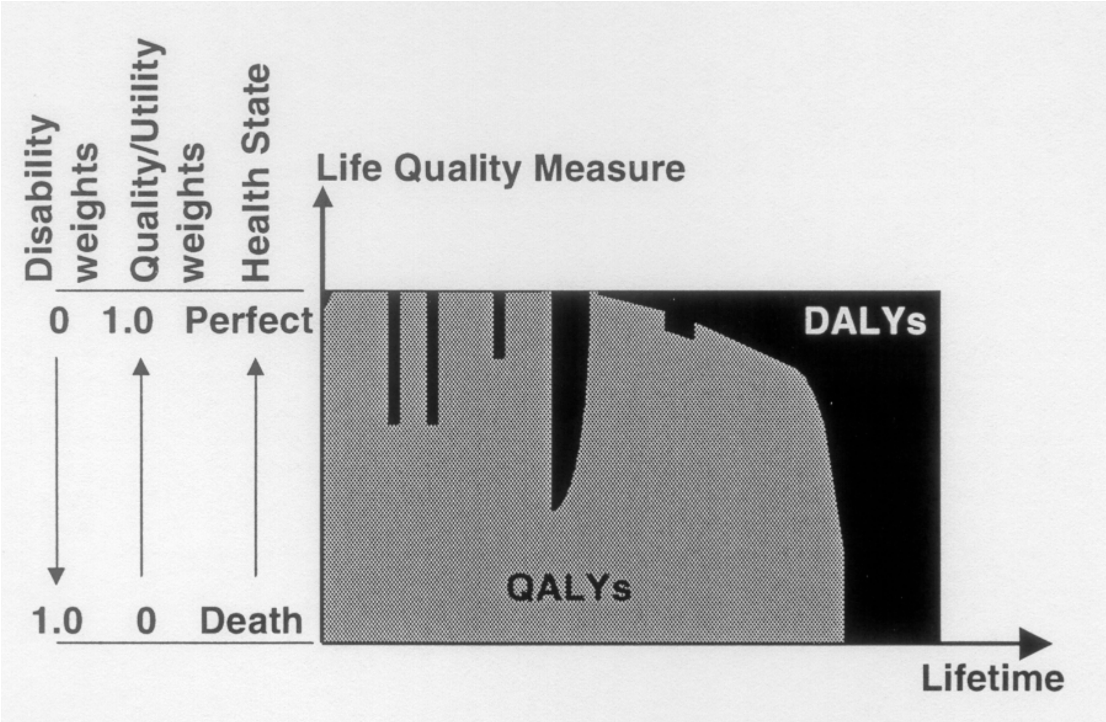


Figure 5. Graphical illustration of DALY and QALY metrics (Source: Hofstetter and Hammitt, 2002)

Figure 5 illustrates the difference in reference point for DALYs and QALYs. Any effective intervention to reduce the number of Campylobacter infections should result in a reduction in DALYs associated with infection and a gain in QALYs. Note that QALYs and DALYs use different scales on the vertical axis.

In the QALY approach, health-related quality of life is expressed in a number between 1 and 0, where 1 corresponds with perfect health and 0 with death. One year of life in perfect health 'produces' 1 QALY, one year of life in a reduced health produces less than 1 QALY and death produces 0 QALYs. As is clear from figure 5, QALYs may also be calculated as the aggregation of different periods with different health-related quality of life.

DALYs are the sum of years of life lost (YLL) and years lived with disability (YLD). The YLL is calculated using standard life expectancy for age and sex. YLD are calculated as a multiplication of disability weight and disability duration. Compared to the quality weights used for QALY calculations, as explained above, disability weights are anchored in the opposite way. Here, 0 refers to perfect health, while 1 refers to death.

In the context of cost-effectiveness analysis, a correction for discounting and age weighting can be applied (Fox-Rushby and Hanson, 2001). This is different from the calculation of DALYs to estimate the burden of disease, as explained in paragraph 4.3.1. When estimating disease burden cross-sectionally, the factor time is irrelevant. However, investments today have economic and health effects in the future. Applying a discount rate is generally used to account for the fact that health today is valued higher than health in the future, and for the fact that there is uncertainty about future possibilities to (better) treat diseases. Age weighting can also be applied because it is unlikely that each of the years of life lost is of equal value, from a societal perspective. In general, society attaches higher values to years of life lost at the age of 30 than at the age of 90. More in-depth information on QALYs, DALYs and their use in economic evaluation can be found in Appendix 1.

Despite the conceptual similarity of DALY and QALY measures, DALYs have so far hardly been used in the context of cost-effectiveness analysis (Fox-Rushby *et al*., 2001). In fact, there is increasing debate about the value of DALYs in decision-making (Fox-Rushby, 2002). Critics point at the fact that use of DALYs has important equity implications and would lead to systematic allocation of resources to interventions targeted at the younger and healthier part of the population. Compared to DALYs, QALYs consider typical age-related disabilities and actual life expectancies and age weighting is not applied. The disability weights to be used in the calculation of DALYs reflect the values of panels of 'experts', rather than preferences from the society at large (see also paragraph 4.5.3). QALYs are therefore less vulnerable in the context of societal decision-making. Also, because there is broad experience with use of QALYs in CEA, more (Dutch) reference data to assess the cost-effectiveness of Campylobacter prevention are available (see e.g. Table 2.19 in Van Oers, 2002). In principle, these reference data facilitate the choice to spend money either on Campylobacter prevention or say, on noise reduction along motorways. Based on these reflections, cost-effectiveness of interventions to prevent human Campylobacteriosis will primarily be presented as cost per life year gained and cost per QALY.

4.5.2 Viewpoint of analysis

From the extensive listing of cost categories that are relevant from a health economist perspective (paragraph 4.3.2) and cost categories relevant for the chicken meat chain (paragraph 4.4.1), it is instantly clear that campylobacteriosis crosses the traditional borders of economic evaluation studies within one sector of society, e.g. health care. Interventions under study in CARMA have (economic) implications for the partners in the food production chain. And although effects may also be realised within the food production chain (e.g. reduced costs of outbreaks for producers), the majority of effects, such as the reduction of gastro-enteritis and associated days lost paid work, will be effectuated in other sectors of society. It is to be expected that most costs will be made in the food production chain, while health care (reduced costs of treatments for human campylobacteriosis), employers (reduced days lost paid work) and society at large (reduced intangible costs) benefit from these investments.

Traditionally, the societal perspective is the principal perspective to choose in economic evaluations. From a societal perspective, investments/interventions are worth doing, when the society as a whole is better off, than when doing nothing[1]. This means that all costs and benefits to society have to be included in the analysis, irrespective of the payer of costs or receiver of benefits. The central question is whether society at large would benefit from the implementation of these interventions. In a following step, decision-makers would then have to apply/develop measures in order to stimulate and compensate the 'losers' and assure their participation. However, this last step is behind the scope of this study. Many examples of interventions that are not beneficial from a health care payer's perspective but beneficial from a societal perspective exist. For instance, influenza vaccination of healthy employees is unattractive for the health care payer, but the monetary value of the expected reduction in days lost paid work is much larger than the costs of vaccination, hence beneficial for society at large. In such situations it is accepted practice to evaluate the intervention from all relevant perspectives. In the case of Campylobacter reduction, interventions will be evaluated from the perspective of (different players in) the chicken meat chain and from the societal perspective separately. Risk managers may then choose the perspective that is most relevant to them.

[1] The theoretical assumption hereby is the Kaldor-Hicks criterion. According to the Kaldor-Hicks criterion, 'a policy that creates gainers and losers in welfare, but if the gainers *could* compensate the losers and remain better off themselves after the change then society as a whole has benefited' (Drummond et al., 1997).

Such disaggregated information is also essential to improve the acceptance of interventions under study.

4.5.3 Disability weights and weighing the quality of life

For both DALY and QALY calculations, a factor describing the level of disability or quality of life, relative to death and perfect health, is needed. Disability weights to use in DALY calculations have so far been based on descriptions of (different stages of) specific disease presented to panels of experts, i.e. health care workers and medical doctors, and thus reflect the values of a limited part of the general population. In the Netherlands, DALYs have been used in a descriptive sense, to compare the burden of diseases relative to each other (Van Oers, 2002). The disability weights were derived from medical doctors (Stouthard *et al*., 2000).

In QALY calculations, weights derived directly from patients, relatives, caregivers, doctors, or the general population have been applied. As was demonstrated by De Wit *et al*. (2000) these different groups tend to value health states differently. In general, patients attach higher values to health states than outsiders do. There is broad international consensus that if QALYs are used in a decision-making context, only general population values should be used (Drummond *et al*., 1997). This consensus is reflected in Dutch guidelines for economic evaluation research (CVZ, 2000). In general, weights to be used in QALY calculations are derived from large population samples. These samples are asked to value hypothetical health states, without explicit reference to (different stages of) specific diseases, as was described above for the derivation of disability weights to be used for DALYs.

Using mathematical modelling techniques, weights for all possible health states between 0 (quality of life equals death) and 1 (quality of life equals perfect health) are derived from the limited number of health states that are valued in those samples. To calculate QALYs for a specified disease stage, actual descriptions of health states of patients are necessary. For all health status measurement questionnaires currently in use, such as EQ-5D, Short-Form 36 and Health Utilities Index, algorithms are available to assess population-based quality weights for the health status of patients.

To calculate QALYs, data on the health status of patients in several stages of disease are needed for the four main outcomes of Campylobacter infection (gastro-enteritis, reactive arthritis, GBS, IBD). Using published algorithms, values can be attached to these health states. For gastro-enteritis, the SENSOR study provides with descriptions of health states of patients. For reactive-arthritis, IBD and GBS it is unknown at present whether health status measurements are available. This will be subject of further study. Should no primary data be available, data from the literature will be used.

4.5.4 Variability and uncertainty

According to Law and Kelton (2000), true validation of a model requires that data on the real system are available. In practice, however, real-life data are often limited and/or absent. Therefore every model builder has to deal with some degree of uncertainty and methodological controversy (Drummond *et al*., 1997). Total uncertainty combines uncertainty and variability (Vose, 2000). A description on the difference between ‘variability’ and ‘uncertainty’ was given in box 1 of paragraph 2.2. Within the CARMA project, the uncertainty and variability around the parameters describing the microbial risk, the effectiveness of intervention measures, the infection incidence of Campylobacteriosis and secondary sequelae, and the illness duration and severity are accounted for by using for each individual parameter a kind of probability distribution, together with repeated runs of the model. With regard to the unit prices for the different cost categories to be considered in the estimation of the cost of illness and the estimation of the chicken meat chain costs triggered by the different intervention measures under study, as well as the estimates about the disability weights, unit prices and weights will be considered in first instances as 'given', using their 'best guess', despite their uncertainty. For example, this means that the volumes of health care use are being treated as variable and uncertain, while unit prices are regarded in the first instance as 'given'.

In a second step, we will then consider explicitly the uncertainty and variability around the 'cost-estimates' e.g. the estimated unit prices to be considered in the estimation of the cost of illness and the estimation of the chicken meat chain costs triggered by the different intervention measures under study, as well as the estimates about the disability weights. By doing sensitivity analysis on these parameters and quantifying the extent of their influence we might identify those 'cost-estimates' that have the greatest influence on the results and conclusions obtained (Belli *et al*., 2001). We will pay special attention to parameters where a possible change of the 'best guess' estimate might result in a different conclusion of our study. When doing sensitivity analysis, values of relevant parameters are systematically varied over some range of interest in order to determine their impact on the results. It is reasonable to vary one parameter at a time, while assuming holding all other parameters unchanged, if each of the parameters is independent of all other parameters. However, if several parameters are correlated, then it is best to estimate several parameters simultaneously (Dijkhuizen and Morris, 1997). In our sensitivity analysis we will, in first instance change wherever possible only one parameter at a time. But, we will consider also the possibility of changing several parameters simultaneously.

In a last step we will consider the model uncertainty, e.g. uncertainty due to necessary simplification of real-world processes. Hereby, our attention will focus more on the assumptions made considering for example possible future developments with regard to the Dutch chicken meat supply and/or with regard to the Dutch demand for Dutch chicken meat.

4.6 Special considerations regarding cost-effectiveness

One complicating factor is that more than 50% of all chicken meat produced in the Netherlands is exported (Havelaar, 2002). This implies that other countries will obtain benefits, in terms of reduced number of human Campylobacter infections and sequelae, because preventive measures have been implemented in the Netherlands. If the only benefits to be valued are the benefits obtained within the Netherlands, the interventions within the chicken meat chain will appear to be less cost-effective. One solution to this problem will be to estimate the cost-effectiveness of interventions assuming that all effects are realised within the Netherlands. Such an analysis will reveal the true effects of interventions, no matter in what country they are realised. Another solution could be to assume that interventions are implemented in the chicken meat chains of all EU countries, while using Dutch data to estimate its costs and effects. Than, effects could be valued at the level of the EU. For such an analysis, import and export data at the level of the EU are needed.

One further factor complicating the estimation of cost-effectiveness, is the fact that it is unknown what the role of co-morbidity and genetic susceptibility to infection is. These two factors may independently affect life expectancy of persons who acquire a Campylobacter infection or who are more prone to develop sequelae. Life-expectancy plays an important role in the calculation of cost-effectiveness, in a sense that the outcome parameters 'life-years gained' and 'quality adjusted life years gained' in general are calculated from standard life tables, reflecting average life-expectancy of both diseased and healthy people. If persons who die from infection with Campylobacter and at the same time have one or more other (severe) diseases or a weak immune system, it is unlikely that the full range of remaining life years to be calculated from standard life tables would apply. However, it is unknown by what factor life expectancy for those people is reduced. Preliminary Danish data showed that life expectancy of Campylobacter-infected persons is average, after correction for concurrent diseases. As already stated in paragraph 4.3, the relevance of these factors will be studied in more detail, and if there are indications that there is a substantial a priori reduction in life-expectancy, this will be incorporated in the calculation of life years gained, and thus in the cost-effectiveness calculations.

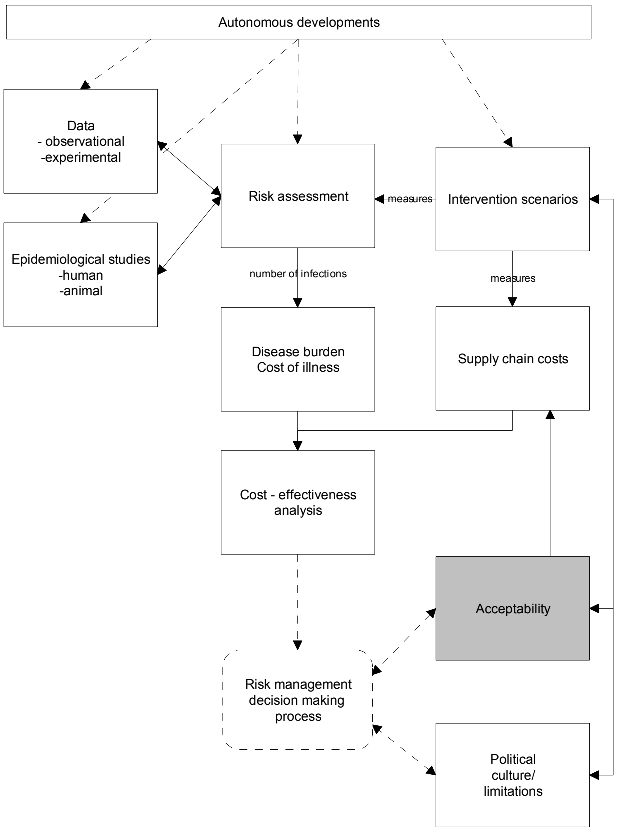
One side-effect of some interventions to reduce Campylobacter infection in the chicken meat chain, such as improved hygiene and decontamination, is that the prevalence of other pathogens will be reduced as well. For instance, it is likely that these interventions will also have an effect on presence of Salmonella. If only effects on Campylobacter reduction are valued, the cost-effectiveness of interventions will be underestimated. However, within the CARMA project, it will not be possible to develop models for both Campylobacter and Salmonella infections. Using data from previous cost of illness estimates for human salmonellosis (van den Brandhof *et al.*, 2003), we will try to quantify the economic benefits of salmonella reduction to a certain extent.

4.7 Presentation of results of economic analysis

The cost-effectiveness of each of the interventions presented in paragraph 2.3 will first be assessed relative to the current situation (year 2000 situation before implementation of interventions). This will point out the interventions that are more and less cost-effectiveness. If possible, the next step will be to make an incremental analysis. This implies that the cost-effectiveness of interventions is assessed when they are implemented on top of each other. First, the most cost-effective intervention is modelled, thereafter the second-most attractive intervention is modelled assuming that the most attractive intervention is already implemented. This allows for the assessment of relative cost-effectiveness of interventions. Several combinations of interventions will be presented, in close co-operation with the risk modellers. However, at present it is unknown whether a true incremental analysis will be possible, because it is doubtful whether effects of interventions are independent.

In performing cost-effectiveness analysis, there is often a difference in timing of costs and effects. Investments now result in cost savings and health improvements in the future. To account for this difference in timing, discounting is applied. This means that costs (savings) and effects that are realised in the future are valued less than those effectuated at present. The rationale for discounting is, among others, that individuals have a preference for health today over health in the future, that there is uncertainty about the future (health problems today could be solved in the future), and that there is diminishing marginal utility to additional life-years. The officially recommended discount rate in the Netherlands is 4 % at present (CVZ, 2000; HAFIR, 2003). The consequence of discounting is that effects that are realised in the (far) future, e.g. after vaccination, are weighted much lesser than effects that are realised today, e.g. surgical procedures. In such situations, discounting has a large influence on the cost-effectiveness of interventions (by making them appear less cost-effective). In order to provide full insight in the effects of interventions, results will be presented both discounted (4% discount rate) and non-discounted. To what extent the discount rate influences the main conclusions of the study will be subject of a sensitivity analysis.

5. Acceptability of interventions



5.1 Introduction

In order to be successful in reducing the number of human Campylobacter infections, interventions should ideally be acceptable to all stakeholders. Here, stakeholders are defined both as actors in the chicken meat chain and consumers. Acceptability of intervention may be expressed by positive opinions, and attitude or behaviour with regard to the measures (Hoogerwerf, 1992). Risk managers should have an understanding of stakeholders' opinions with respect to measures. Interviews of stakeholders can provide with these insights.

5.2 Stakeholder analysis: interviews and workshop

Within the CARMA project, insight in stakeholders' opinions was gained through a stakeholders analysis performed in 2001. This analysis consisted of a rough exploration of relevant actors, the selection of stakeholders, mobilising of stakeholders and interviews with representatives of selected organisations. Finally a workshop with stakeholders was organised (Bogaardt *et al.*, 2002). Besides the two Ministries involved, representatives of conventional chicken producers, of 'ecological' chicken producers, of processing plants, of butchers, of retailers, and of consumers took part in the stakeholders' analysis. No individual consumers or supermarkets participated. Therefore, the stakeholders' analysis is neither representative nor exhaustive. A criterion was that players in the chicken meat chain, including consumers, were approached and invited that were expected to be most affected by the intervention measures under consideration. Researchers made the choice and then the selection was presented to risk managers for approval. The results of the stakeholders' analysis form a qualitative image of the opinions dominating among Dutch stakeholders within the chicken meat chain. Besides the stakeholders analysis, an industry forum has been set up which acts as a sounding board for input about the effectiveness of intervention measures.

5.3 Discussion of the results of the stakeholder analysis

The stakeholder analysis showed that although almost every stakeholder recognises i.e. says that the contamination of chicken meat with Campylobacter is a serious problem, the seriousness of the problem is not fully internalised. This aspect has to do with the acceptability of the problem that depends on the perception of the seriousness of the problem, the extent in which industry and consumers are willing to do something to solve the problem, the extent in which for example a chicken producer meets difficulties due to the problem of chicken being infected with Campylobacter. Another aspect of acceptability deals with government intervention. For many years, government has given full responsibility to industry to solve the problem of Campylobacter themselves. Ultimately, when results failed to occur, Dutch government threatened industry with serious bans. Currently, industry expects the government to act as initiator and financier of research on Campylobacter. However, industry prefers to remain responsible for the determination of the measures to be taken. Industry still sees the role of the government more in supporting (financially) then interfering.

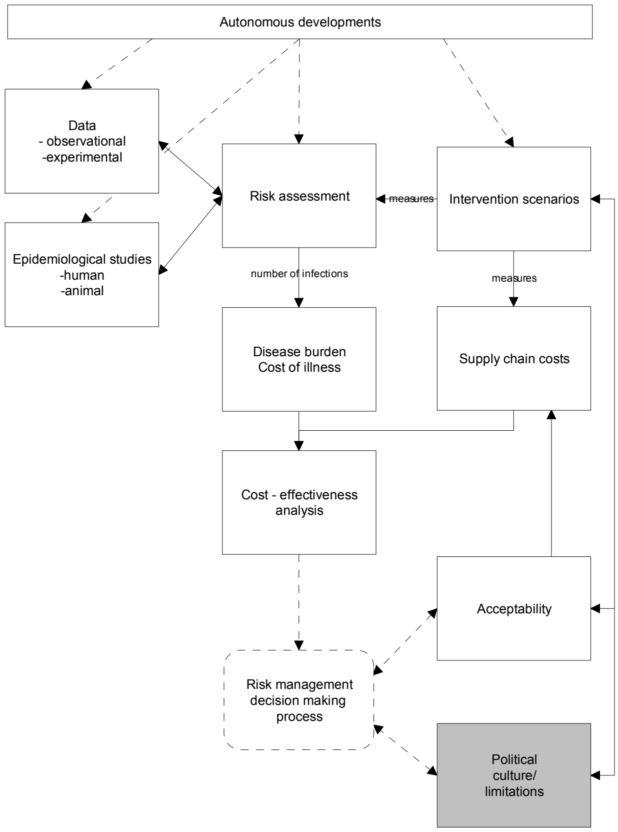
Furthermore the stakeholders analysis made clear that to a large extent there is agreement on the norm. The national government states that food products 100 percent free of pathogens will never be achievable. Therefore, the government acclaimed the so called 0+ % norm, implying that meat should be almost 100 % free of pathogens, but that some Campylobacter in or on chicken meat may still be present. This aspect shows that acceptability also deals with the goal of public policy. Acceptability of the norm depends on the justification and feasibility of the norm. For example: Are there enough opportunities to realise the norm? Has industry enough confidence in scientific evidence with regard to the norm? These issues will affect future discussion on the plus behind the zero: will this be 0.5 or 2%?

Also the analysis showed that the industry had not agreed with the implementation of the warning sticker on pre-packed chicken meat. Furthermore the interviews showed that industry and government agree that intervention measures should be taken in all stages of the chicken meat chain, from chicken meat farmers to consumers. Stakeholder's opinion on what measures should be taken and the effectiveness of measures deals with questions like: are industry and consumers of the opinion that the measures and the desired changes will indeed lead to a useful / meaningful contribution to the solution of the problem? According to industry and consumers, does a measure fit into the present business culture? Are stakeholders of the opinion that they will be affected disproportionally? Concerning the acceptability of the measures under consideration the analysis showed that the industry argues that an important condition for implementing measures is its proven functioning and that government and most stakeholders agree with decontamination as an alternative measure. However, consumers may have major concerns about irradiation and may not be ready for the introduction of irradiated chicken meat products (Swabe, 2001:32-33).

An aspect that was not taken into account in the stakeholder analysis was the acceptability of government actions when measures are implemented in practice. This aspect of acceptability deals with the expectations of the industry and consumers with regard to the implementation. The question is: do the industry and consumers expect that controlling organisations have sufficient knowledge that they act precisely, that they have sympathy for problems occurring in the implementation phase?

In future phases of the CARMA project, more extensive participation of stakeholders within the chicken meat chain, especially from the side of consumers and retailers will be sought. In order to get more quantitative insight into opinions and behaviour of individual Dutch consumers, chicken meat farmers, slaughterhouses and supermarkets, a questionnaire will be administered in these groups.

6. Political culture of risk managers



One of the aims of the CARMA project is to provide insight in the cost-effectiveness of interventions to reduce Campylobacter infection in humans. The underlying aim of such analyses is to assist in the process of rational decision making. According to theory, risk managers with a given and limited budget should start selecting those interventions with the lowest cost-effectiveness ratios, than select interventions with slightly higher cost-effectiveness ratios, and so on, until the budget is used. By following this principle, the maximum benefit given the limited budget will be realised. However, the reality is entirely different from the process described above. Many policies already implemented have never been assessed for their cost-effectiveness. Also, although league tables ordering interventions for their cost-effectiveness suggest differently, CEAs are not always comparable because of methodological differences. And in the real world, many other arguments besides cost-effectiveness play a role in decision-making, such as equity arguments and public concern around a certain health problem. In the real world, risk managers may choose not to implement relative cost-effective interventions on the one hand, while at the same time deciding to implement interventions with unfavourable cost-effectiveness.

Here, it is interesting to note that the two departments that are mainly involved in food safety issues (including campylobacteriosis), namely the Ministry of Health, Welfare, and Sports and the Ministry of Agriculture, Nature, and Food Quality have different cultures with regard to the role that is played by economic evaluation research in decision making. From the second half of the 1980s, cost-effectiveness has been an issue in decisions of the Ministry of Health on new public health programs. For instance, the decision to start with a cervical cancer screening program was taken after a careful evaluation of its cost-effectiveness. Also, new vaccination programs were assessed for their cost-effectiveness. At the Ministry of Agriculture on the contrary, the concept of cost-effectiveness has so far received less attention. Formal cost-effectiveness analyses have hardly been used for policy making in this field. Until the last decades of the twentieth century, policy-making for animal disease control in most countries was dominated by veterinary advice, whereby disease control was often perceived as 'an all-or-nothing affair' (Dijkhuizen *et al*., 1995). The motivation for eradication of endemic diseases was to reduce production losses (e.g. eradication of foot-and-mouth, control of brucellosis) and/or to prevent infection in humans (e.g. brucellosis). In the 1970s, the first economic evaluations were performed. These first analyses were applied from the perspective of the single farmer at herd level, using partial budgeting techniques, and later from the perspective of the industry (farmers, slaughterhouses and processing industry), using cost-benefit techniques. The access to export markets with a higher disease-free status, mostly coupled with higher prices for the producers, was and is the driving force. The target beneficiary of animal health policy was so far mostly the commercial livestock sector. Within the field of animal health economics, only a few and more recent economic evaluations were applied from a societal perspective, such as Andersson *et al*., 1997; Garner *et al*., 1995a&b; Mahul *et al*., 1999; and Mangen *et al*., 2002. However, large epidemics of infectious animal disease, such as the classical swine fever in 1997/98 in the Netherlands, the foot-and-mouth epidemic in 2001 in the United Kingdom, as well as the on-going epidemic of avian influenza in the Netherlands (June 2003), and other crises like the BSE crisis in 1996, which all received huge media attention, have lead to a transformation from more technical related questions on animal disease control into politically sensitive issues. Current FAO programmes in veterinary public health and food safety aim to establish cost-effective control of zoonotic diseases (FAO, 2003).

Because more economic evaluation studies have been performed so far in the (public) health field, more reference data are available. In the most recent Public Health Status and Forecasts (VTV) report, a table with cost per QALY of about 30 interventions from both the environmental and health field is published (van Oers *et al*., 2002). This table distinguishes groups of programs with similar cost-effectiveness ratios, ranging from low-cost-programs to programs that cost more than € 1 million per QALY. Within the health field, differences with regard to the 'acceptable' level of cost-effectiveness seem to exist for curative and preventive programs. In general, a higher amount per QALY is accepted for curative interventions. For preventive healthcare programs, the unofficial but widely accepted threshold is around € 20.000 per QALY (Simoons and Casparie, 1998). Of course, not all programs with better cost-effectiveness are reimbursed, as sometimes programs with worse cost-effectiveness are implemented. Another important argument is the total budgetary impact of a program: is additional money to fund a program available? A further argument seems to be the (individual) burden of disease. For interventions targeted at diseases with severe consequences for quality of life (such as transplantations for patients with severe stages of pulmonary emphysema), higher cost-effectiveness ratios are accepted in general than for public health programs, such as vaccination and population screening.

Interventions to prevent Campylobacter infections are different from the health care programs described above, in a sense that the costs and effects of interventions are not realised within one sector of society. Groups that benefits from the interventions (e.g. public health) are not necessarily those who incur the costs (e.g. chicken producers and/or chicken meat processing plants). Identifying those who will gain, those who will pay, and those who will lose gives the analyst and/or the decision-maker insight into the incentives that various stakeholders have to implement the interventions, and to support it or oppose it (Belli *et al*., 2001). This means that within the CARMA project, full attention should be paid to the acceptability of interventions for the different stakeholders within the chicken meat chain and the maintenance of (less popular) interventions. As well as the requirement that investment/intervention should improve the welfare of society at large, investments/interventions should be financially viable, recurrent costs should be met, and the distribution of costs and benefits (monetary or in terms of additional gained life years and/or better health) should be acceptable to society (Belli *et al*., 2001).

Appendix 1: QALYs versus DALYs and their use in economic evaluation

Two metrics that are often used to combine morbidity and mortality are quality adjusted life years (QALYs) and Disability Adjusted Life Years (DALYs). One advantage of the use of such metrics is that diseases and/or interventions can be made comparable across each other. DALYs are often used to provide insight into the burden of different diseases. QALYs are often used to evaluate interventions for one or more different diseases. The CARMA project will use QALYs to compare alternative interventions for reducing *Campylobacter* in chicken meat and DALYs to estimate the disease burden of human campylobacteriosis and its serious disease sequelae.

QALYs aggregate the actual health quality over time, DALYs aggregate the loss of health compared to perfect health. DALYs and QALYs complement each other during a typical course of life, as is demonstrated in the figure below. Note that QALYs and DALYs fill the rectangular box (representing a lifetime) and do not overlap.

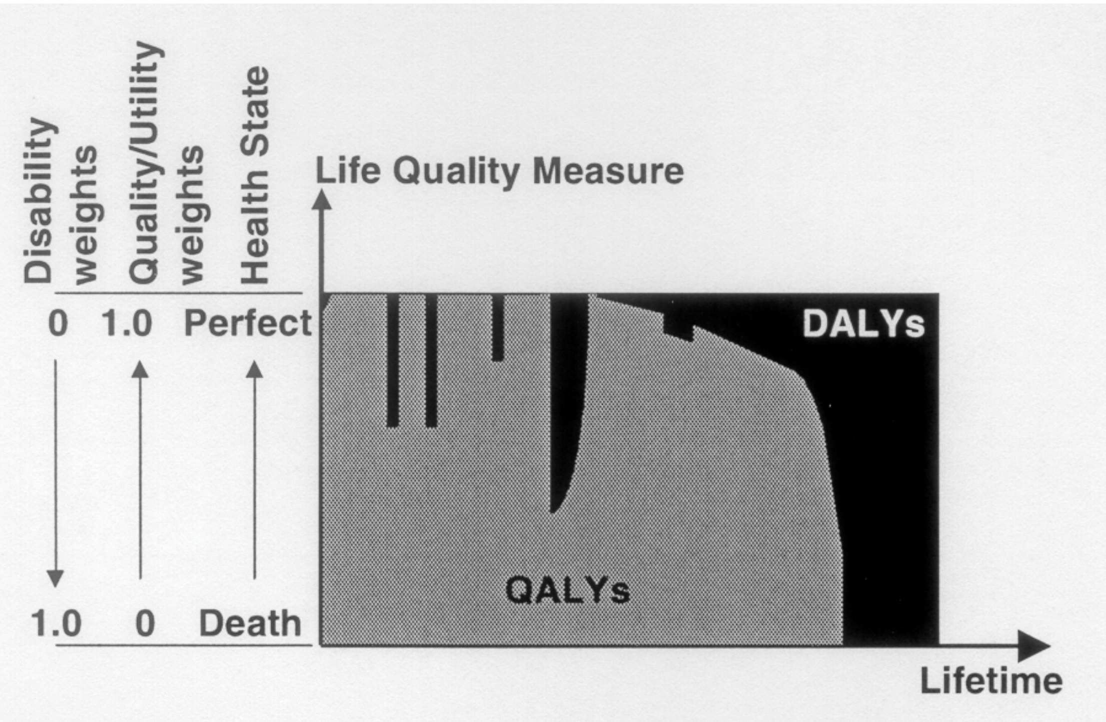


Figure A1. Graphical illustration of a health profile and its measurement by quality adjusted life years (QALYs, gray area) and disability adjusted life years (DALYs, black area) (Source: Hofstetter and Hammitt, 2002)

What QALYs and DALYs have in common is the use of a ‘weight’ to correct for a health state that is less than perfect. This weight is either called a disability weight (using DALYs) or a quality weight (using QALYs). The weights for QALYs and DALYs are shown on the vertical axis. A chronic disease with a severe impact on quality of life (like severe schizophrenia) would e.g. have a disability weight of 0.8, on a scale of 0 (perfect health state) to 1 (death). Correspondingly, this severe disease state would be valued with a quality weight of 0.2, on a scale of 0 (death) to 1 (perfect health state).

The figure above illustrates the difference in reference point for DALYs and QALYs. Any effective intervention to reduce the number of Campylobacter infections should result in a reduction in DALYs associated with infection and a gain in QALYs, respectively. One year of life in perfect health "produces" 1 QALY, one year of life in a reduced health produces > 0 and < 1 QALY and death produces 0 QALYs. As is clear from the figure, QALYs may also be calculated as the aggregation of different periods with different health-related quality of life.

DALYs are the sum of years of life lost (YLL) and years lived with disability (YLD). The YLL is calculated using standard life expectancy for age and sex. YLD are calculated as a multiplication of disability weight and disability duration. A numerical example demonstrates the calculation of both DALYs and QALYs.

Let us assume a 60 year old person who has his first heart attack, after a life in perfect health. The normal life-expectancy would be 80 years. This person medical care immediately after his heart attack and survives the attack. Without this medical treatment, the heart attack would have killed him at age 60. He now enters a health state that is less than perfect, being a heart patient taking medication for the rest of his life, with diet restrictions and the awareness that a second heart attack is possible. Let us assume that this health state is valued at 0.9 (in the QALY system, i.e. at 90 % of normal) and at 0.1 in the DALY system. A second and fatal heart attack occurs at the age of 70.

The number of DALYs lost from heart disease is:

Years of life lost = (80-70) + Years lived with disability = (10 * 0.1) = 11 DALYs.

The number of QALYs gained from the high quality interventions immediately after his first heart attack is: 10 years * 0.9 life quality = 9 QALYs.

The fact that DALYs and QALYs complement each other (at least in this simplified way to calculate them) can be demonstrated from the fact that 11 DALYs and 9 QALYs fill the 20 year time period between 60 and 80 years.

However, if measuring the cost of an intervention against what you gain, the gain in QALYs is similar to the reduction in DALYs due to the intervention. The gain in QALYs due to standard care after a heart attack was calculated above as 9 QALYs. In this case, what is the reduction in DALYs due to the intervention whose cost-effectiveness is being measured? As stated above, this person would have died from his heart attack at the age of 60 without medical care, resulting in a loss of 20 DALYs. Without the intervention, the number of DALYs lost is 11, as demonstrated above. Therefore, reduction in DALYs due to the intervention is 9, as is the gain in QALYs. Provided that the disease and quality weights that are attached to a certain health state are complementary along the 0 to 1 spectrum, an economic evaluation using DALYs as outcome measure should have results identical to one using QALYs as outcome measure. However, this simplified numerical example ignores an array of methodological differences between both methods.

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