RISK RANKING: ESTIMATES OF THE BURDEN OF FOODBORNE DISEASE FOR NEW ZEALAND

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SUMMARY

This report contributes to a project with the following goal:

- The development of a single metric of risk ranking that can be applied to both chemical and microbiological hazards, and is applicable to the varied risk ranking needs of the NZFSA.

From 2002 – 2005 the risk ranking project conducted by ESR for the NZFSA developed a process, and used expert opinion to produce severity and incidence estimates for a number of food/(microbiological) hazard combinations.

A previous report from this project in the current financial year (FW06109) discussed the available metric options, and chose the disability adjusted life year (DALY) as the most appropriate single metric.

The approach used in developing DALY estimates for New Zealand has been strongly guided by estimates prepared for the Netherlands in 2006 (Kemmeren *et al.*, 2006). Further details were found in specific Dutch estimates for *Campylobacter* (Havelaar *et al.*, 2000) and shiga-toxin producing *Escherichia coli* (STEC) (Havelaar *et al.*, 2004).

For this project, development of DALY estimates for the following illnesses was agreed with the NZFSA:

- Campylobacteriosis
- Salmonellosis
- Listeriosis (invasive, perinatal and non-perinatal)
- Infection with STEC
- Yersiniosis
- Infection with Norovirus

A significant proportion of these illnesses are caused by foodborne transmission of the pathogens (typically 40-90+%, depending on the pathogen).

Of the six potentially foodborne microbial diseases examined in the current exercise the highest ranked issue, according to the DALY approach is *Campylobacter* infection, followed by norovirus infection, perinatal listeriosis, *Salmonella* infection, *Yersinia* infection, STEC infection and acquired (non-perinatal) listeriosis.

However, estimates associated with different organisms vary widely in their degree of associated uncertainty. For example, the model used to calculate DALYs associated with norovirus infection generates a 95% confidence interval for the total number of gastroenteritis cases that spans three orders of magnitude, while the total range of mean DALY values for all diseases considered only covers two orders of magnitude.

1 INTRODUCTION

This report contributes to a project to rank the risks associated with pathogens in food, with the following goal:

- The development of a single metric of risk ranking that can be applied to both chemical and microbiological hazards, and is applicable to the varied risk ranking needs of the NZFSA.

From 2002 – 2005 the risk ranking project conducted by ESR for the NZFSA developed a process, and used expert opinion to produce severity and incidence estimates for a number of food/(microbiological) hazard combinations (Cressey and Lake, 2003; 2004a; b; 2005b). The challenge is now to rank these, by devising a single metric that describes the burden of disease by combining information about severity and incidence. A further challenge will be to devise this metric in a way that is also applicable to chemical hazards. The health effect most commonly associated with foodborne microbiological hazards is acute gastrointestinal disease; chemical hazards cause a wider variety of adverse health effects, usually after exposure over a much longer time period and are not further discussed in this report.

The purpose of this risk ranking exercise is to assist the NZFSA Science Group in setting priorities, particularly in relation to the Domestic and Imported Food Reviews.

A previous report from this project in the current financial year discussed the available metric options, including economic approaches such as cost, cost effectiveness and cost utility, and chose the disability adjusted life year (DALY) as the most appropriate single metric (Lake, 2006). The DALY approach was chosen as this approach appears to provide the best measure of individual and societal burden of disease. The DALY was also specifically designed to estimate burden of disease in an international context, and this should permit comparison with overseas estimates. The International Collaboration on Enteric Disease Burden of Illness Studies has recently established a DALY Working Group to explore the methodology and the potential for an estimation of the global burden of foodborne disease.

The approach used in developing DALY estimates for New Zealand has been strongly guided by estimates prepared for the Netherlands in 2006 (Kemmeren *et al.*, 2006). Further details were found in specific Dutch estimates for *Campylobacter* (Havelaar *et al.*, 2000) and STEC (Havelaar *et al.*, 2004).

Discounting is a methodology used in economic analysis to compare costs that occur over an extended period of time on the basis of present value (Kemmeren *et al.*, 2006). At this stage, the issue of discounting for future illness has not been addressed.

2 DALY ESTIMATES: GENERAL CONSIDERATIONS

Disability adjusted life years (DALYs) were originally developed by the World Health Organization for the Global Burden of Disease Study (Murray and Lopez, 1997). In relation to foodborne disease, they have been most extensively used for the Netherlands (Kemmeren *et al.*, 2006; Mangen *et al.*, 2004).

The following material is taken from Kemmeren *et al*. (2006). The fundamental calculation for DALYs is:

$$DALY = YLL + YLD$$

YLL is the number of years of life lost due to mortality and YLD is the number of years lived with a disability, weighted with a factor between 0 and 1 for the severity of the disability (d).

The YLL due to a specific disease in a specified population is calculated by the summation of all fatal cases (n) due to the health outcomes (l) of that specific disease, each case multiplied by the expected individual life span (e) at the age of death.

$$YLL = \sum_{l} n_l \times e_l$$

YLD is calculated by accumulation over all health outcomes (l), the product of the number of cases (n), the duration of the illness (t) and the severity weight (w) of a specific disease. It should be noted that the calculation for YLL implicitly includes a severity weight factor. The severity weight or disability weight factors are in the range zero to one, with the severity weight for death being equal to one.

$$YLD = \sum_{l} n_l \times t_l \times w_l$$

Information on the incidence of illness and death is derived from clinical, epidemiological and surveillance studies, whereas information on severity weights is typically derived from elicitation of special panels, preferably from the general population.

3 ILLNESSES, OUTCOMES, AND SEVERITY WEIGHTINGS

For this project, development of DALY estimates for the following illnesses was agreed with the NZFSA:

- Campylobacteriosis
- Salmonellosis
- Listeriosis (invasive, perinatal and non-perinatal)
- Infection with shiga-toxin producing *Escherichia coli* (STEC)
- Yersiniosis
- Infection with Norovirus

According to an expert consultation conducted for a risk ranking process in 2005, a significant proportion of these illnesses are caused by foodborne transmission of the pathogens (40-90+%) (Cressey and Lake, 2005b).

A detailed description of the process to model the DALY burden for each illness is provided in Appendices 1-7. This section provides a generalised overview of the approach taken.

The DALY estimates were calculated by developing a model using @RISK software (Palisades Corporation). For many of the factors needed for the calculations there were differing data sources or methods of estimation. These were used to describe distributions to encompass the uncertainty in the estimates. Details of model inputs are given in Appendices 1-7.

3.1 Outcomes

The adverse health outcomes resulting from these illnesses define the components of the DALY estimate. It is essential to define the specific outcomes for each illness.

The principal outcome for these illnesses (except listeriosis) is acute gastrointestinal illness (AGI), with varying degrees of severity. The illness is usually self-limiting, i.e. people recover by themselves, and any treatment is usually limited to rehydration solutions, pain killers, or anti-diarrhoea medicines. Patients may obtain these as over-the-counter medicines, or else from a visit to a health professional, usually a general practitioner (GP).

Although *Listeria monocytogenes* infection may cause a non-invasive febrile gastroenteritis, there are no reliable data on the incidence and severity of this disease, and this project only considered the invasive form of the illness.

The severity or duration of AGI is usually reflected in the actions taken by or for patients, and in occasional circumstances may result in death. We define the outcomes of AGI as:

- Self limiting – recover by themselves, do not visit GP.
- Visit a GP
- Hospitalised
- Death

In this study it was assumed that cases who were hospitalized would have previously presented to a GP. This was also the approach taken in the Dutch study (Kemmeren *et al.*, 2006).

For some illnesses, further categories of AGI outcome may be needed e.g. for infection with STEC, AGI with or without bloody diarrhoea may occur.

For a small proportion of cases with AGI, longer-term illnesses (sequelae) may follow the initial infection. These sequelae result in a range of disabilities and may also result in death. In some cases, the sequelae of a microbial disease may be an identified risk factor for subsequent disease. For example, inflammatory bowel disease has been associated with an increased risk of developing bowel cancer (Ekbom *et al.*, 1990). However, the current study follows the approach of Kemmeren *et al*. (2006) in only including diseases that are recognised as direct sequelae to the microbial disease.

The specific outcomes included in the DALY estimates for each illness are defined in the following sections. In general, these follow the approach used by Kemmeren *et al*. (2006).

3.1.1 Campylobacteriosis

The outcomes are:

AGI:

- AGI (do not visit a GP and recover)
- AGI (visit a GP and recover)
- AGI (hospitalised and recover)
- AGI (death)

Campylobacteriosis Sequelae:

- Guillain Barré Syndrome (GBS) (subcategories of mild, severe, and fatal)
- Reactive arthritis (ReA) (subcategories of no GP visit, GP visit, and hospitalised)
- Inflammatory Bowel Disease (IBD)

Inflammatory bowel disease (IBD) is a collective term used to describe a group of chronic intestinal diseases of the bowel. The two most common IBDs are Crohn's disease (CD) and ulcerative colitis (UC). Estimates of cases of IBD made in this study are based on the study of Gearry *et al*. (2006), which classified cases of IBD as either Crohn's disease, ulcerative colitis or indeterminate colitis.

3.1.2 Salmonellosis

The outcomes are:

AGI:

- AGI (do not visit a GP and recover)
- AGI (visit a GP and recover)
- AGI (hospitalised and recover)
- AGI (death)

Salmonellosis Sequelae:

- ReA (subcategories of no GP visit, GP visit, and hospitalised)
- IBD

3.1.3 Listeriosis (perinatal)

A review of the literature for the Netherlands study indicated that the adverse outcomes for the foetus of *Listeria* infection in the mother were:

- Abortion, still birth
- Liveborn infected: severe systemic infection, sepsis, pneumonia, CNS infection (meningitis)

Due to a lack of information on liveborn listeriosis cases, the Dutch study based their DALY estimate for perinatal listeriosis only on deaths. The same approach was taken in the current study.

3.1.4 Listeriosis (acquired, non-perinatal)

For *Listeria* infection in persons other than pregnant women a wider range of outcomes were considered by the Dutch study:

- Visit a GP and recover
- Visit a GP and hospitalised, experience gastroenteritis and recover
- Visit a GP and hospitalised with septicaemia and recover
- Visit a GP and hospitalised with septicaemia and die
- Visit a GP and hospitalised with meningitis and recover
- Visit a GP and hospitalised with meningitis and die
- Visit a GP and hospitalised with meningitis and experience long term neurological sequelae
- Visit a GP and hospitalised and die

These outcomes were condensed into the following categories:

- Sepsis
- Meningitis
- Gastroenteritis
- Pneumonia
- Long term neurological sequelae
- Death

3.1.5 STEC infection

A complex set of outcomes were considered by the Dutch study for the consequences of STEC infection. These were condensed in the analysis to the following categories:

- Gastroenteritis with non-bloody diarrhoea

- Gastroenteritis with bloody diarrhoea
- Gastroenteritis with fatality
- Haemolytic uraemic syndrome (HUS)
- End Stage Renal Disease (ESRD), subsequent to HUS, including disability and/or death due to dialysis, transplantation and graft rejection

3.1.6 Yersiniosis

This illness was not considered in the Dutch study. We consider that the same AGI outcomes will apply. A range of complications for infection with *Yersinia enterocolitica* were reported from a nine year study in the Netherlands (Stolk-Engelaar and Hoogkamp-Korstanje, 1996). These included enteritis, enteritis with complications (including septicaemia, lymphadenitis, arthritis, erythema nodosum, and disturbed liver function), appendicular syndrome, ileitis, and colitis.

The outcomes selected for this study are:

AGI:
- AGI (do not visit a GP and recover)
- AGI (visit a GP and recover)
- AGI (hospitalised and recover)
- AGI (death)

Yersiniosis Sequelae:

Although there are a range of complications resulting from yersiniosis, as an interim position, it was decided to only estimate reactive arthritis as a sequel contributing to the DALY burden, due to a lack of information on the incidence and severity of other sequelae. This is also in agreement with the symptoms described in a Dutch publication on diet and safe food which incorporates the Campylobacter Risk Management and Assessment (CARMA) project (in Appendix 5) (van Kreijl *et al.*, 2006).

- ReA

3.1.7 Norovirus infection

Sequelae are not considered to occur following norovirus infection. The outcomes are simply those for AGI.

AGI:
- AGI (do not visit a GP and recover)
- AGI (visit a GP and recover)
- AGI (hospitalised and recover)
- AGI (death)

3.2 Severity Weightings

There are no New Zealand specific severity/disability weightings available for the outcomes discussed in Section 3.1. The Ministry of Health estimate of the burden of disease and injury

in New Zealand (Tobias, 2001) used disability weights principally from the Netherlands and Australia.

A list of disability weights used in the Netherlands for all of the outcomes relevant to this study is provided in the CARMA report on priority setting of foodborne illnesses (Kemmeren *et al.*, 2006). Values used have been reproduced from Kemmeren *et al*. (2006) (Table 3) unless otherwise indicated (Table 1).

Table 1: Disability weight for disease states relevant to potentially foodborne infectious intestinal disease

Illness	Disability weight#
Death	1.00
AGI (do not visit a GP and recover)	0.067
AGI (visit a GP and recover)	0.393
AGI (hospitalised and recover)	0.393
GBS (mild)*	0.10 – 0.30
GBS (severe)*	0.44 – 0.80 – 0.94
ReA (not visiting a GP)	0.127
ReA (visiting GP)	0.21
ReA (hospitalised)	0.37
IBD	0.26
STEC: Gastroenteritis with non-bloody diarrhoea**	0.067
STEC: Gastroenteritis with bloody diarrhoea**	0.393
HUS**	0.90
Listeriosis: gastroenteritis	0.01
Listeriosis: Sepsis	0.93
Listeriosis: Meningitis	0.32
Listeriosis: Pneumonia	0.04
Listeriosis: Long term sequelae	0.25

Kemmeren *et al*. (2006)

* Actual values used were further refined using time course of the illness. Recovery from the illness was modeled by defining a time period and modeling the decrease in the disability weight over that time period.

** (Havelaar *et al.*, 2004)

The use of point disability weights is a simplification, as in reality the descriptors in the left hand column of Table 1 will encompass a range of disabilities. It is interesting to note that the disability weights make distinctions between three severities of acute gastroenteritis. Gastroenteritis due to *Listeria monocytogenes* infection is considered to be very mild and unlikely to influence activities of daily life (ADL). AGI due to other organisms, not requiring a GP visit, receive a higher disability weighting suggesting that AGI of this sort with have

some impact on ADL. Non-bloody diarrhea due to STEC infection is classified as equivalent to non-GP visit AGI, although a study has indicated that 22% of STEC cases with non-bloody diarrhea will present to medical authorities (Michel *et al.*, 2000). AGI requiring a GP visit, with or without subsequent hospitalization is considered to severely impact on ADL. STEC infection with bloody diarrhea is given an equivalent disability weighting, which seems reasonable as the study of Michel *et al*. (2000) reported that 73% of STEC cases with bloody diarrhea will present to medical authorities.

3.3 Duration of Illness

3.3.1 AGI

The duration of episodes of gastrointestinal illness is considered to be a function of the severity of the illness (see Table 2). Values from previous studies relevant to this project are summarised in Table 2 for comparison purposes. The estimates for the previous New Zealand study (Lake *et al.*, 2000) were largely based on data provided by standard texts, except for hospitalised cases, which were based on New Zealand Health Information Service (NZHIS) records of actual cases.

Table 2: Duration of disease estimates for gastroenteritis associated with potentially foodborne infectious intestinal diseases

AGI Category	New Zealand (Lake *et al.*, 2000) (days)	Netherlands (Kemmeren *et al.*, 2006) (days)
Campylobacteriosis		
No GP visit	5	3.48
GP visit	5	9.72
Hospitalised	7.4	14.39
Salmonellosis		
No GP visit	3.5	5.58
GP visit	3.5	10.65
Hospitalised	10	16.15
Listeriosis–non perinatal		
No GP visit	45.4	7.3 (0.02 years x 365)
GP visit	45.4	7.3 (0.02 years x 365)
Hospitalised	45.4	7.3 (0.02 years x 365)
STEC infection		
No GP visit	6	3 (non bloody diarrhoea)
GP visit	6	5 (bloody diarrhoea)
Hospitalised	7.8	N/A
Yersiniosis		
No GP visit	9	N/A
GP visit	9	N/A
Hospitalised	11	N/A
Norovirus infection		
No GP visit	2	3.8
GP visit	N/A	5.7
Hospitalised	N/A	7.2

N/A = not applicable

Duration data from Kemmeren *et al.* (2006) were used wherever available for the current study. These data are generally similar to those used by Lake *et al*. (2000), with the exception of the duration figures for *Listeria*.

3.4 Life expectancy

The Demographic Trends 2006 report from Statistics New Zealand (http://www.stats.govt.nz/analytical-reports/dem-trends-06/default.htm) provides tables that show life expectancy for males and females at ages up to 90 years, for the years 2000-2002. These were used for calculations in these DALY estimates.

3.5 The AGI "pyramid"

AGI and its consequences can be organised into a pyramid which expands through the sequence:

- **Mortality**
- **Long term sequelae**
- **Hospitalisations**
- Notifications
- Laboratory confirmed cases
- Cases who visit a GP and supply a faecal sample
- Cases who visit a GP and who are requested to supply a sample
- **Cases who visit a GP**
- **All cases (GP visitors and community cases)**

The DALY method requires estimation of the number of cases at each of the bolded levels. However, the primary dataset we have used concerns notifications. Consequently there is a need to apply scaling factors to the number of notifications to estimate the number of laboratory-confirmed cases, and then to apply another scaling factor to estimate the number of cases attending a GP and finally to apply another scaling factor to estimate the total number of cases.

Many of the estimations have been handled as Pert distributions of (minimum, most likely, maximum). For salmonellosis and yersiniosis notifications, data from 1997 to 2005 were used as the source. The most likely value was chosen as the number of notifications from 2005, the most recent reported year, while minimum and maximum were set as the highest and lowest numbers during that period. Campylobacteriosis was treated slightly differently; as the incidence of this illness has increased markedly over the last 5-10 years, the minimum and maximum values were selected from the years 2001-2005.

Corrections for undernotification have been applied, using data that compared the number of laboratory confirmed cases with the number of notifications in Auckland in 2000 (Simmons *et al.*, 2002). The correction factor to scale up the number of notifications to the number of laboratory confirmed cases has been applied as a Pert distribution using the proportion and the 95% confidence interval of this proportion for each illness (Table 2; Simmons *et al*., 2002).

To scale up from the number of laboratory cases to the number of cases visiting a GP it is necessary to estimate the number of cases presenting to a GP from whom a faecal sample is requested. This has been estimated from a survey of GPs conducted in 1995 (Sarfati *et al.*, 1997). The 135 GPs who responded to the survey indicated that, of patients with AGI over 5 years of age, 42% of GPs would request a stool sample from less than 25% of cases, 31% of GPs would request samples from 25-50% of cases, and 23% of GPs would request samples from more than 50% of cases. These percentages add up to 96%, but it was further reported that 9.6% of GPs sent a stool specimen to the laboratory for every patient with acute gastroenteritis. We have scaled back the other percentages proportionally to accommodate this value. Thus the percentages of patients from whom a stool sample is requested is 0-24% (39.6% of GPs), 25-50% (29.2% of GPs), 51 – 99% (21.5% of GPs), 100% (9.6% of GPs). For modeling purposes, the ranges are treated as uniform distributions and each range selected according to the percentages of GPs, using the RiskDiscrete Function. So that this factor can be applied to each iteration in the model, this factor was simulated independently to generate a mean probability that a GP will request a stool sample (p = 0.416).

The total number of cases (those who present to a GP and those who do not, i.e. community cases) has been scaled up from either the number of notified cases, the number of laboratory confirmed cases, or the number of cases presenting to a GP. A number of papers from overseas provide information that allows estimations of these ratios for each illness, and in some cases more than one estimate is possible. Where more than one estimate is possible, they have been treated as the limits of a uniform distribution.

The number of community cases not attending a GP has been determined by subtracting the number of GP cases from the total number of cases.

Hospitalisations, and long term sequelae have been estimated using a variety of literature sources. For some estimates, the incidence of these outcomes have been estimated as a proportion of the number of cases notified, presenting to a GP or in the community. For others, data on hospitalisations have been segmented to estimate the number of cases with a relevant infectious antecedent.

Kemmeren *et al*. (2006) used the data from Helms *et al*. (2003) to estimate the excess mortality in a 12 month period following infection by several zoonotic bacteria. While a similar approach is theoretically possible for New Zealand, the study of Helms *et al*. (2003) did not include all organisms included in the current study and so cannot be applied to all the illnesses for which DALY estimates are required. For consistency, the current study has based the numbers of deaths on actual identified fatalities, from either EpiSurv or NZHIS records. The Dutch approach, based on Helms *et al*. (2003) produces much higher estimates of the number of fatalities. For example, application of this approach to *Campylobacter* in New Zealand would produce an estimate of more than 30 deaths per annum subsequent to *Campylobacter* enteritis, as compared with recorded deaths with a mean of 1.2 per annum.

3.6 Data from New Zealand Health Information Services (NZHIS)

A data request was submitted for hospitalised cases and mortality for the set of relevant ICD –10 codes listed in Appendix 8. The most up to date data were obtained: 2000 – 2006 hospitalisations) and 2001 – 2004 (mortality). The data request included cases where the ICD code occurred anywhere in the first 20 diagnosis codes.

In most cases matching of disease states of interest with ICD-10 code was straightforward. The major exception was reactive arthritis, for which there is no specific ICD-10 code. The codes matched to this disease were selected after consultation with specialists (see Appendix 8).

To determine the number of cases in a year for each illness from the NZHIS data, readmissions within the same calendar year were removed.

3.7 Timeframe

The intention in developing these estimates was to describe the burden of illness using the most recent data. Inevitably the years for which the most recent data were available varied amongst the data required.

A second consideration was that DALY estimates can be strongly affected by rare events amongst the New Zealand population e.g. disease specific mortality. Whether or not deaths had occurred due to a particular illness in a specific year could change the estimates considerably. The approach taken for such components of the burden of illness was to generate distributions that described the incidence of such outcomes over a period of several years, usually the years 2000-2005. This also enabled the production of distributions such as age ranges for cases involved in such rare events.

Almost all of the data used for these DALY estimates were derived from the years 2000-2005.

3.8 Attribution: Percentage Foodborne

The proportion of the DALY burden of illness estimates attributed to foodborne transmission of the pathogens has been calculated using attribution estimates provided by an expert consultation workshop conducted in May 2005 (Cressey and Lake, 2005b). The mean values for the expert estimates of minimum, most likely, and maximum were treated as a Pert distribution for modeling purposes. The relevant data for the illnesses being considered are given in Table 3.

Table 3: Proportion of disease due to foodborne transmission – summary of expert opinion, May 2005 (Cressey and Lake, 2005a)

Disease	Minimum (%)	Most Likely (%)	Maximum (%)
Campylobacteriosis	37.1	57.5	69.6
Salmonellosis	45.4	60.7	68.9
Listeriosis	78.4	84.9	92.1
STEC infection	27.0	39.6	51.4
Yersiniosis	41.5	56.2	70.8
Norovirus infection	27.9	39.6	48.9

The panel from whom these data were elicited included 14 experts in food microbiology, clinical microbiology, epidemiology or public health. Opinions were collected by application of a two pass modified Delphi, with a facilitated discussion between the first and second application of the elicitation questionnaire. Results in Table 3 are from the second pass.

4 RESULTS: DALY ESTIMATES

Details of information sources used and the modelling approach taken for each of the potentially foodborne microbial diseases considered in this study are outlined in Appendices 1-7.

Table 4 summarises the results of the simulation run for the DALY model in @Risk (10,000 iterations). For convenience, mean values for YLD, YLL, DALYs and foodborne DALYs are consolidated in Table 5.

Table 4: Summary results – Disability Adjusted Life Years (DALYs) for major foodborne infectious intestinal diseases in New Zealand

Disease State	Incidence (Cases per year)			YLD	YLL	DALYs	
	Mean	5th percentile	95th percentile			Total	Foodborne
Campylobacteriosis							
GE, total	**123,000**	**89,000**	**170,000**	**508**	**30**		
GE, no GP	81,000	41,000	126,000				
GE, GP only	42,000	37,000	46,000				
GE, Hospitalisation	950	710	1260				
GE, Death	1.3	0.4	2.3				
GBS, total	**28**	**24**	**32**	**186**	**18**		
GBS, mild	5.6	4.5	6.6				
GBS, severe	23	19	26				
GBS, death	1	0.6	1.5				
ReA, total	**3,200**	**2,400**	**4,000**	**290**			
ReA, no GP	2,500	1,800	3,250				
ReA, GP	540	200	950				
ReA, Hospitalisation	135	24	320				
IBD, total	**49**			**535**			
Total				**1506**	**48**	**1554**	**880**
Salmonellosis							
GE, total	**16,800**	**5,800**	**29,800**	**66**	**46**		
GE, no GP	12,400	1,500	24,600				
GE, GP only	4,400	3,500	5,700				
GE, Hospitalisation	159	119	214				
GE, Death	2.4	0.5	4.6				
ReA, total	**365**	**184**	**582**	**27**			
ReA, no GP	288	142	467				
ReA, GP	62	19	122				
ReA, Hospitalisation	16	2	40				
IBD, total	**4**			**47**			
Total				**140**	**46**	**186**	**111**
Listeriosis (Perinatal)							
Sepsis	1.2	0.7	1.9				
Meningitis	0.4	0.2	0.7				
Pneumonia	1.2	0.6	1.8				
Death							

Disease State	Incidence (Cases per year)			YLD	YLL	DALYs	
	Mean	5th percentile	95th percentile			Total	Foodborne
- perinatal - neonatal	2.5 0.4	1.4 0.2	3.8 0.7				
Neurological sequelae	0.2	0.1	0.4				
Total				**0.5**	**228**	**229**	**195**
Listeriosis (Acquired)							
Sepsis	4.9	3.4	6.7				
Meningitis	7.5	5.5	10.1				
Gastroenteritis	3.6	2.4	5.1				
Pneumonia	3.6	2.4	5.1				
Death	1.4	0.5	2.3				
Neurological sequelae	1.0	0.8	1.4				
Total				**5**	**21**	**26**	**22**
STEC infection							
GE, total	**340**	**180**	**620**	**1.0**	**33**		
GE, bloody	148	96	202				
GE, non-bloody	192	15	505				
GE, death	0.7	0.2	1.5				
HUS, total				**0.5**	**26**		
HUS, clinical	9.3	4.9	16.9				
HUS, death	0.4	0.2	0.8				
ESRD	**1.2**	**0.6**	**2.2**	**16.6**	**14**		
Total				**18**	**73**	**91**	**35**
Yersiniosis							
GE, total	**7,900**	**5,700**	**10,400**	**57**	**29**		
GE, no GP	6,600	4,500	9,000				
GE, GP only	1,300	1,200	1,450				
GE, Hospitalisation	37	30	41				
GE, Death	0.5	0.1	1.2				
ReA, total	**80**	**50**	**115**	**7**			
ReA, no GP	63	38	92				
ReA, GP	14	5	25				
ReA, Hospitalisation	3	1	8				
Total				**64**	**29**	**93**	**52**
Norovirus infection							
GE, total	**403,000**	**71,000**	**1,004,000**	**530**	**6**		
GE, no GP	357,000	43,000	942,000				
GE, GP only	46,000	7,000	116,000				
GE, Hospitalisation	18	10	27				
GE, Death	0.8	0.2	1.4				
Total				**530**	**6**	**536**	**210**

GE = gastroenteritis GP = general practitioner GBS = Guillain-Barré Syndrome
ReA = Reactive Arthritis IBD = Inflammatory Bowel Disease
HUS = Haemolytic Uraemic Syndrome ESRD = End Stage Renal Disease

Key points to note from the DALY simulation include:

- Sequelae (GBS, ReA, IBD) account for two-thirds of the total DALYs for campylobacteriosis. For ReA and IBD, number of cases have been calculated by applying factors derived overseas to the total number of campylobacteriosis cases. These figures should be viewed with some caution unless they can be validated for New Zealand.
- Similarly, sequelae (ReA, IBD) account for 40% of the total DALYs for salmonellosis. Fatalities contribute significantly (25%) to the total salmonellosis DALYs.
- Fatalities are the main determinants of total DALYs for both perinatal and acquired listeriosis, and STEC infection. For perinatal listeriosis and STEC infection this is due to the fact that fatalities are more likely to be in younger cases, while for the other microbial diseases considered, fatalities are more likely to be older cases.
- For yersiniosis, the relatively long time course of AGI is a major determinant of total DALYs. Consequently, although the mean number of cases of yersiniosis is less than half that for salmonellosis, the DALYs associated with non-fatal AGI are similar.
- The DALY estimate for norovirus infection is mainly determined by the large number of community cases of AGI. However, the estimate of the number of cases is extremely uncertain.

Table 5: Mean YLD, YLL, DALYs and foodborne DALYs for potentially foodborne infectious intestinal diseases in New Zealand

Disease	YLD	YLL	DALYs	Foodborne DALYs (5^{th}-95^{th} percentile)
Campylobacteriosis	1506	48	1554	880 (586-1174)
Norovirus infection	530	6	536	210 (51-462)
Listeriosis, perinatal	0.5	228	229	195 (110-290)
Salmonellosis	140	46	186	111 (68-177)
Yersiniosis	64	29	93	52 (24-85)
STEC infection	18	73	91	35 (24-70)
Listeriosis, acquired	5	21	26	22 (8-45)

Basing the estimate for norovirus infections on multiplications up from New Zealand notified cases may overestimate the incidence, since at the time of the UK IID study (which provides the multipliers) norovirus detection was by electron microscopy. This method is likely to be less frequently applied than the more recent PCR technique. It is possible that the base number of notifications in the IID study is lower than would be expected today, due to this methodological difference. The PCR technique is likely to enhance the identification of norovirus cases creating a higher base figure in recent New Zealand notifications.

An alternate approach to estimating the burden of disease from norovirus infections is to use the population based rates found in the UK IID study (Wheeler et al., 1999). These were: community cases 1,250 per 100,000 (95% CI 940 - 1,670), and GP cases 199 per 100,000 (95% CI 145 - 273). These estimates were applied as Pert distributions (along with the 7 March 2006 census night New Zealand population of 4,143,279) to replace the estimates of GP and community cases. This gave a mean of 61,182 cases, (5 and 95 percentiles 51,910 and 70,912 respectively). These figure provide estimates of YLD = 96, and YLL = 2, giving

a total DALYs of 98, and foodborne DALYs of 37. This would significantly change the rank position of norovirus infection, on the basis of DALYs.

Stored samples from the UK IID study have been reanalysed using PCR techniques (Amar *et al.*, 2007). Of 2,422 cases samples, 871 (36%) were positive for norovirus by PCR, compared to 154 found positive by electron microscopy (EM). However, the number of positive control samples also increased from 6 by EM to 358 (16%) by PCR. Given the high level of asymptomatic carriage of norovirus DNA it is uncertain how these data could be used to improve estimates of AGI due to norovirus.

5 DISCUSSION

Application of the DALY approach to potentially foodborne infectious intestinal disease in New Zealand allows a ranking of food safety issues. Of the six potentially foodborne microbial diseases examined in the current exercise the highest ranked issue, according to the DALY approach is *Campylobacter* infection, followed by perinatal listeriosis, norovirus infection (depending on the method used to calculate the total number of cases), *Salmonella* infection, *Yersinia* infection, STEC infection and acquired listeriosis. *Campylobacter* ranks highly due to its high incidence, but also because of the range and seriousness of its sequelae. The ranking for perinatal listeriosis is based entirely on the number and age of fatalities, resulting in a large number of years of life lost, while the ranking of norovirus infection is due to the large number of cases estimated.

However, estimates associated with different organisms vary widely in their degree of associated uncertainty. For example, the model used to calculate DALYs associated with norovirus infection generates a 95% confidence interval for the total number of gastroenteritis cases that spans three orders of magnitude, while the total range of mean DALY values for all diseases considered only covers two orders of magnitude.

Decisions made in the construction of the model can have major impacts on the final DALY value. Two-thirds of the DALY estimate for *Campylobacter* is due to the long term sequelae that can result from infection (Guillain-Barré Syndrome, reactive arthritis and inflammatory bowel disease). While the evidence used to extrapolate from reported *Campylobacter* cases to unreported *Campylobacter* cases and to sequelae is the best currently available, in most cases it is not New Zealand specific and it is possible that patterns of illness in New Zealand may be different to those observed overseas.

The DALY modeling also required something of a mosaic approach, with the approach to a particular organism being dictated by the available information. For example, for *Campylobacter* and *Salmonella* studies were available that related the number of notified or laboratory–confirmed cases to the estimated total cases (Kemmeren *et al.*, 2006; Wheeler *et al.*, 1999), whereas for STEC infection this extrapolation was not possible and reported presentation rates from outbreaks were used (Michel *et al.*, 2000). This mosaic approach means that model uncertainties will originate from different sources depending on the organism.

Despite these shortcomings, the DALY approach provides a useful mechanism for assimilating a huge amount of information on infectious intestinal diseases, that would otherwise not be comparable, to produce a single metric suitable as an input to risk prioritization.

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APPENDIX 1 BACKGROUND INFORMATION – CAMPYLOBACTERIOSIS

Acute Gastroenteritis

The only systematic source of information on campylobacteriosis cases in New Zealand is the national surveillance database (Episurv) maintained by ESR. Entries to the database represent cases notified by health professionals and recorded by Public Health Units. The number of laboratory positive stool tests has been shown to exceed the number of notified cases. Based on a one-year study of GP notifications carried out in Auckland (Simmons *et al.*, 2002) it has been estimated that the proportion of laboratory confirmed campylobacteriosis cases actually notified is 76% (95% CI 75% - 78%). These values were used as a Pert distribution to scale up the number of notifications to the number of laboratory confirmed cases.

The number of laboratory confirmed cases was converted to the number of GP cases using the stool requesting frequencies of New Zealand GPs as described in Section 3.5. This approach estimates approximately 2.4 cases attending a GP for every laboratory confirmed case.

The estimated ratio of total GP cases to laboratory confirmed cases for New Zealand is consistent with overseas estimates. A Dutch study estimated that the total number of campylobacteriosis cases attending a GP would be 2.3 times the number of laboratory confirmed cases (Kemmeren *et al.*, 2006), while a UK study estimated that GP cases were 2.4 times laboratory confirmed cases for *Campylobacter* (Wheeler *et al.*, 1999).

Not all cases of campylobacteriosis will result in a GP visit. Community studies are generally recognised as the best means of estimating the total burden of acute gastrointestinal disease. ESR are currently conducting for the NZFSA New Zealand's first nationwide community study of acute gastrointestinal illness (AGI). However, while this will give an estimate of the total AGI burden in New Zealand, it will not allow estimation of the total number of campylobacteriosis cases.

Overseas studies have made various estimates of the proportion of total campylobacteriosis cases that will result in a GP visit. A Dutch study estimated that 24% of gastroenteritis cases caused by *Campylobacter* would result in a GP visit, based on community-based studies (Kemmeren *et al.*, 2006), while a UK study estimated that 47.1% of campylobacteriosis cases would consult a GP (Wheeler *et al.*, 1999).

These two values were used as the limits of a uniform distribution to provide a factor by which the estimated number of campylobacteriosis cases visiting a GP in New Zealand was scaled up to estimate the total number of cases. The difference between the estimated total number of cases and GP visits was calculated to give the number of community (AGI, no GP visit) cases.

It was assumed that cases hospitalised due the *Campylobacter* infection will have presented to a GP and are likely to have had a stool sample submitted for laboratory testing. While some cases with *Campylobacter* infection may present directly to hospital accident and emergency departments and be admitted, the current study assumed that this was not common. Kemmeren *et al*. (2006) used a case control study of laboratory-confirmed campylobacteriosis patients to estimate that 9% of laboratory-confirmed cases of campylobacteriosis in the Netherlands would be hospitalised. Based on 2005 New Zealand

notification data and the under-notification study of Simmons *et al*. (2002), this approach would lead to an expectation of approximately 1500 hospitalisations due to campylobacteriosis in New Zealand. In the 2005 year, the Episurv database contained records of 635 campylobacteriosis cases being hospitalised in New Zealand.

The Notifiable Diseases Summary report for 2005 includes a table based on NZHIS data that indicates 871 hospitalisations (principal diagnosis) and 199 hospitalisations (other diagnosis) (ESR, 2006).

New Zealand hospital discharge records obtained for this project give a slightly different estimate with 858 hospitalised *Campylobacter* cases in 2005, based on the primary diagnosis code only and adjusting for readmissions. If the appearance of the ICD 10 code for *Campylobacter* enteritis in any diagnosis code field is considered then the number of hospitalized cases increases by 174 for 2005 to 1032.

These estimates were used as the basis for a Pert distribution for hospitalisations: (635, 871, 9% of estimated laboratory confirmed cases).

The annual number of fatalities due to *Campylobacter* infection in New Zealand has varied between zero and three (2000) with a mean of 1.2, according to the Episurv database. For the current study the number of fatalities was modeled as a Pert distribution, with a most likely value of 1.2, a minimum of 0 and a maximum of 3.

A distribution was fitted to the ages of all reported campylobacteriosis fatalities in New Zealand (1997-2005) and values were drawn from this distribution and combined with life expectancy table for New Zealand to estimate the number of years of life lost due to campylobacteriosis-related fatalities.

The duration of campylobacteriosis is related to the severity of the illness. Kemmeren *et al*. (2006) used British data to assign duration values to community cases, not attending a GP (3.48 days), GP cases, not hospitalised (9.72 days) and hospitalised cases (14.39 days). While these figures were used for the current analysis, it should be noted that, while the Dutch study reported an average hospital stay of 5.9 days for hospitalisation due to 'other bacterial pathogens', analysis of New Zealand hospital discharge data indicates an average length of stay for cases with *Campylobacter* enteritis as the primary diagnosis code of 2.77 days. It is uncertain whether this is indicative of a shorter duration of such campylobacteriosis cases in New Zealand or differences in hospital practices. In addition this does not account for the period of illness before and after hospitalisation. Consequently, the duration of illness for hospitalised campylobacteriosis was not adjusted down from 14.39 days.

Guillain-Barré Syndrome (GBS)

Lake *et al*. (2000) assumed that 25% of GBS cases could be attributed to prior infection with *Campylobacter jejuni*, based on overseas studies (Hahn, 1998; Rees *et al.*, 1995). The crude annual incidence of GBS has been estimated for a number of countries to be in the range 0.8-2/100,000 (Van Koningsveld *et al.*, 2000). This suggests an annual number of GBS cases for New Zealand of 32-80, with *Campylobacter*-related cases of 8-20. Analysis of New Zealand hospital discharge records for 1988-2006 revealed annual numbers of hospitalised GBS cases to actually be in the range 60-109, with the number of cases in 2005 being 101 (Lake *et al.*, 2004).

A review of a hospital discharge series in southwest Netherlands found that 116/615 (18.9%) of patients discharged with a diagnosis of GBS did not meet clinical criteria (Van Koningsveld *et al.*, 2000). A UK study found evidence of recent *C. jejuni* infection in 26% of a case series of 103 patients with confirmed GBS (Rees *et al.*, 1995). A further UK study estimated a lower proportion of GBS cases due to prior *C. jejuni* infection of 15% (Tam *et al.*, 2003). However, this study made no clinical connection between the *C. jejuni* and GBS cases.

A number of estimates have been derived of the probability of developing GBS subsequent to a *C. jejuni* infection. In the UK the probability of developing GBS within 2 months of *Campylobacter* enteritis was estimated to be <2/10,000 (Tam *et al.*, 2006), while a Swedish study made a higher, but similar estimate of GBS following *C. jejuni* infection of 3.04/10,000 (95% CI 1.39-5.78) (McCarthy and Giesecke, 2001). The annual estimate of 115,000 campylobacteriosis cases in New Zealand (Lake *et al.*, 2000), would suggest 22-35 *Campylobacter*-related GBS cases for New Zealand per annum.

The severity of GBS can be expressed in terms of an F-score, with scores ranging from 0 = Healthy to 6 = Dead (Havelaar *et al.*, 2000). For GBS, an F score <3 (able to walk without assistance) is considered to be mild, while an F-score of 3 (able to walk with assistance) or greater is considered to be severe (Havelaar *et al.*, 2000). Van Koningsveld *et al*. (2000) reported that 121/436 (28%) of a discharge case series in the Netherlands were mildly affected at the nadir of the disease, while 316/436 (72%) were severely affected.

Amongst mildly affected cases, 21% showed serological evidence of a previous *C. jejuni* infection, while 33% of severe cases showed evidence for a previous *C. jejuni* infection (Van Koningsveld *et al.*, 2000). These figures, when combined, suggest that 23.8% of all GBS cases will be severe cases linked to *Campylobacter* infection and 3.9% will be mild cases linked to *Campylobacter* infection. The total proportion of *Campylobacter*-linked cases (27.7%) is similar to the 25% assumed by Lake *et al*. (2000). Severe GBS is more common in older cases.

Note that further analysis of the above Dutch data on mild and severe cases with *C. jejuni* antecedent infection to account for characteristics of testing procedures (Havelaar *et al.*, 2000) resulted in adjustment to 22% of mild cases, and 38% of severe cases.

A case fatality ratio of 3.4% was employed by Kemmeren *et al*. (2006) for GBS cases. Based on the calculations for New Zealand outlined above, this would equate to approximately one *Campylobacter*-associated GBS fatality in New Zealand per annum. The total number of fatalities due to GBS in New Zealand during the years 2000-2004 was in the range 2-7 (mean = 4.4). If one in four GBS cases is due to prior *Campylobacter* infection these figures are consistent with the analysis outlined above. For the current project a case fatality ratio of 3.4% was used, with the number of years of life lost modeled by simulating the age of GBS fatalities in New Zealand and using New Zealand life expectancy tables to calculate the number of years of life lost.

GBS is self-limiting, with the worst symptoms experienced within a month of the onset of disease (Mangen *et al.*, 2004). However, 15-20% of GBS patients are left with permanent neurological problems, with increasing age being significantly associated with a poor prognosis (Mangen *et al.*, 2004). The time course of the disease is dependent on both the age

of the patient and the initial severity of the illness. For the current study a Dutch model was utilised (Havelaar *et al.*, 2000; Mangen *et al.*, 2004). In this model improvements in the patient's condition are reflected in changes in the disability weighting during the first year after the onset of the illness, and in terms of residual symptoms for the balance of the patients life. Changes in the severity of the illness, and relative proportions of cases in each severity state are used to derive composite disability weight distributions during the first year, and for following years, for both mild and severe cases (Havelaar *et al.*, 2000).

The incidence and age of cases of this illness were modelled as follows.

Overall incidence (from New Zealand hospital discharge data): Pert (60, 101, 109)

This incidence was segmented into mild and severe cases by multiplying the incidence by Beta distributions for Binomial probabilities derived from the proportions 121 mild and 316 severe cases amongst 436 overall cases. The incidence was further segmented into the proportion caused by antecedent *Campylobacter* infection: 22% and 38% for mild and severe cases respectively.

The severe cases were further segmented into cases of age <50 using a Pert distribution derived from the 5 percentile, mean and 95 percentile distribution reported for the Netherlands (Havelaar *et al.*, 2000), and those of age >50 by difference.

The number of deaths from GBS was obtained by multiplying the total number of mild and severe cases by the probability of death derived from the Dutch study (3.4% of 476 cases = 16, Beta (17, 461)) (Van Koningsveld *et al.*, 2000).

The years of life lost to GBS mortality was modelled by determining the life expectancy of the actual 22 cases coded to GBS in NZHIS data from 2000-2004 (almost all of whom were over 60 years of age), and fitting a distribution (Pearson).

The YLD for GBS cases were determined for the first year of illness, and following years, using the above incidence estimates, and the disability weight distributions previously derived for the Netherlands (Havelaar *et al.*, 2000). The number of following years was estimated by fitting the age distribution of cases from New Zealand hospital discharge data provided by NZHIS. The sampled age of the case was then compared to life expectancy tables to obtain the duration of illness.

Reactive Arthritis

A New Zealand case series of 60 reactive arthritis (ReA) found *C. jejuni* to be the organism implicated in triggering the condition in two cases (3.3%) (Highton and Priest, 1996). However, it is unknown what the incidence of ReA is in New Zealand. A European case series of 52 ReA cases did not find evidence of *Campylobacter* as the triggering organism in any instance (Fendler *et al.*, 2001).

A Finnish retrospective study found that 45/609 (7%) of a case series of patients with *Campylobacter*-positive stools fulfilled diagnostic criteria for ReA (Hannu *et al.*, 2002). This was similar to the findings of Johnsen *et al*. who found three cases of ReA in a case series of 37 *Campylobacter* infections (8%) (Johnsen *et al.*, 1983). Another study of 173 *Campylobacter* cases found that 16% met their criteria for ReA (Locht and Krogfelt, 2002).

A much lower figure (2.8%) reporting rheumatologic symptoms following *Campylobacter* infection was found in a Californian study (Rees *et al.*, 2004). This lower figure is very similar to that reported from a case series of 340 patients in Finland (2.4%) (Kosunen *et al.*, 1980).

Kemmeren *et al.* (2006) adopted the data from Hannu *et al*. (2002) and assumed that 7% of cases consulting a GP for campylobacteriosis would develop ReA. They also considered two alternative scenarios in which 7% of all campylobacteriosis cases developed ReA or 7% of only laboratory-confirmed campylobacteriosis cases developed ReA. The results of Hannu *et al*. (2002) were used to estimate that 22% of ReA cases triggered by *C. jejuni* would visit a doctor, while 2.2% would be hopitalised (Kemmeren *et al.*, 2006).

The model for this project has assumed that ReA cases are a subset of those visiting a GP (for campylobacteriosis), and used the data from Finland (45/609) to provide a Beta distribution for the proportion. Of the 45 cases in Finland, 9 had visited a physician because of arthritis, and one was hospitalised for the condition, and these data were used in Beta distributions to estimate the number of cases visiting a GP or hospitalised in New Zealand. The number of cases not visiting a GP nor hospitalised, and visiting a GP but not hospitalised, were calculated by difference.

The duration of illness was based on the exponential expression derived for the Dutch study, using the time course of ReA from several studies, and the disability weights were taken from the analysis conducted in the same study (Kemmeren *et al.*, 2006).

Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is a collective term used to describe a group of chronic intestinal diseases of the bowel. The two most common IBDs are Crohn's disease (CD) and ulcerative colitis (UC). The incidence of IBD in Europe has been reported to be 5.6/100,000 (95% CI: 2.8 to 8.3) for CD and 10.4 (95% CI 7.6-13.1) for UC (Mangen *et al.*, 2004). The Netherlands has been reported to have a higher incidence of IBD at 17/100,000, with approximately 60% of the incidence due to ulcerative colitis.

For the period 1969-1978, New Zealand was reported to have an average incidence of CD of 1.75/100,000 and UC of 5.5/100,000 (Sonnenberg, 1986). A localised study in Canterbury found a considerably higher incidence of IBD of 25.2/100,000 (95% CI 20.8-30.2), with the incidence of Crohn's disease approximately twice that of ulcerative colitis (Gearry *et al.*, 2006). Given reports of upwards trends in IBD worldwide and the relative consistency of the Canterbury study with rates in Europe, the rates reported by Gearry *et al*. (2006) were generalised to represent the New Zealand population.

The additional risk of developing IBD following a laboratory confirmed *Campylobacter* infection has been reported to be 11.46 (Mangen *et al.*, 2004). The age specific incidence rates of IBD reported by Gearry *et al*. (2006) were multiplied by 11.46, then multiplied by the age specific number of notified cases of campylobacteriosis for 2005, and summed across all age groups to give an estimate of the number of IBD cases due to *Campylobacter* infection. The duration of the disease was calculated by combining data on the age distribution of notified campylobacteriosis cases with New Zealand life expectancy data.

In the Dutch study, IBD symptoms were assumed to persist throughout life, but not to impact on the life expectancy of the case (Kemmeren *et al.*, 2006).

Model outputs are summarised in Table 6.

Table 6: Model outputs for campylobacteriosis

Disease State	Incidence (Cases per year)			YLD	YLL	DALYs	
	Mean	5th percentile	95th percentile	Mean	Mean	Total	Foodborne
Campylobacteriosis							
GE, total	**123,000**	**89,000**	**170,000**	**508**	**30**		
GE, no GP	81,000	41,000	126,000				
GE, GP only	42,000	37,000	46,000				
GE, Hospitalisation	950	710	1260				
GE, Death	1.3	0.4	2.3				
GBS, total	**28**	**24**	**32**	**186**	**18**		
GBS, mild	5.6	4.5	6.6				
GBS, severe	23	19	26				
GBS, death	1	0.6	1.5				
ReA, total	**3,200**	**2,400**	**4,000**	**290**			
ReA, no GP	2,500	1,800	3,250				
ReA, GP	540	200	950				
ReA, Hospitalisation	135	24	320				
IBD, total	**49**			**535**			
Total				**1506**	**48**	**1554**	**880**

APPENDIX 2 BACKGROUND INFORMATION SALMONELLOSIS

Acute Gastroenteritis

Annual notified cases of salmonellosis in New Zealand have been in the range 1000-2500 during the last decade, with 1383 cases notified in 2005, the latest reported year (ESR, 2006).

Based on a one-year study of GP notifications carried out in Auckland (Simmons *et al.*, 2002) it has been estimated that the proportion of laboratory confirmed salmonellosis cases actually notified is 82% (95% CI 77% - 85%). These values were used as a Pert distribution to scale up the number of notifications to the number of laboratory confirmed cases.

The number of laboratory confirmed cases was converted to the number of GP cases using the stool requesting frequencies of GPs as described in Section 3.5 and based on the New Zealand study of Sarfati *et al*. (1997). While there is considerable GP to GP variability, it appears that clinical samples are submitted for laboratory confirmation for approximately 40% of cases presenting with symptoms of acute gastroenteritis (Sarfati *et al.*, 1997) (although these data are now somewhat dated). These studies suggest a mean number of salmonellosis cases attending a GP in New Zealand for the 2005 year of 4216.

The Dutch disease burden study estimated a most likely ratio of 5.56 community cases (no GP attendance, 30,000 cases) for every case attending a GP (5,400 cases) (Kemmeren *et al.*, 2006). Overall the number of AGI cases in total was estimated as 35,000, a multiplier of 6.48 compared to the 5,400 GP visiting cases. Based on this ratio the most likely number of community cases in New Zealand would be 23,440, giving a total number of salmonellosis cases of 27,656. A British study of community rates of infectious intestinal disease found a lower ratio of community to GP cases, with 72.7% of salmonellosis cases presenting to a GP, with the total number of salmonellosis cases being approximately 3.2 times the notified rate (Wheeler *et al.*, 1999). This approach would suggest a total of only 4,425 salmonellosis cases in New Zealand. Lake *et al*. (2000) estimated 9,218 salmonellosis cases for New Zealand, with 2,172 of these visiting a GP. Estimates of total salmonellosis cases in Australia produced a median estimated number of 91,974, which pro ratas to approximately 18,000 cases for New Zealand (Hall, 2004).

There is no clear mechanism to indicate which of these approaches would best extrapolate to the New Zealand situation. An approach of 'maximum uncertainty' was taken with the total number of salmonellosis cases in New Zealand being modeled as a uniform distribution between (notified cases x 3.2) and (GP cases x 6.48).

The number of community cases not visiting a GP was determined by difference.

In 2005, the New Zealand national surveillance system reported 142 hospitalisations due to *Salmonella* enteritis (ESR, 2006). This is consistent with information from hospital discharge records, with 130 patients discharged during 2005 having *Salmonella* infection listed in the primary diagnosis code. During the last five reported years, hospitalisations due to salmonellosis reported through the national surveillance system have ranged from 109 to 279 cases. The surveillance figure for 2005 (142) was used as our most likely estimate of hospitalised salmonellosis cases, while the range from previous years was used to define a Pert distribution.

Lake *et al*. (2000) estimated a duration of illness for salmonellosis of 3.5 days for non-hospitalised cases and 5 days hospitalised plus another 5 days pre and post-hospitalisation for hospitalised patients. New Zealand hospital discharge data for 2002/2003 show a mean stay for patient with *Salmonella* infections of 3.8 days (http://www.nzhis.govt.nz/stats/tables/discharges20022003.xls). Kemmeren *et al*. (2006) used a figure of 5.58 days for salmonellosis cases not attending a GP, 10.65 days for cases attending a GP only and 16.15 days for hospitalised cases. The Dutch figures were used for the current study.

With the exception of the 2000 year, when 7 deaths due to salmonellosis were recorded in the national surveillance system, reported fatalities have been in the range 0-2 per annum during the last five years, with one fatality reported in 2005. Lake *et al*. (2000) estimated a mean number of salmonellosis fatalities for New Zealand of 0.7 per annum. A Danish registry-based study determined the relative mortality of 46,212 patients with infectious intestinal disease in the 12 months following laboratory confirmation (Helms *et al.*, 2003). For 25,246 *Salmonella* infection cases, the relative mortality compared to matched controls was 2.85 (95% CI 2.56-3.17). Applying this approach to the New Zealand situation, the median number of excess deaths in the 12 months following laboratory-confirmed *Salmonella* infection would be 17. However, as the study of Helms *et al*. (2003) did not cover all organisms included in the current study, a more conservative approach will be taken and only deaths directly due to salmonellosis were included. For the current study, the number of *Salmonella*-associated fatalities was modeled as a pert distribution, with a most likely value equal to the average number of annual fatalities since 1997 (1.8) and minima and maxima equal to the lowest (0) and highest (7) numbers of fatalities reported during that period. A distribution was fitted to the ages of all reported salmonellosis fatalities in New Zealand (1997-2005) and values were drawn from this distribution and combined with life expectancy table for New Zealand to estimate the number of years of life lost for each fatality modelled.

Reactive Arthritis

A study carried out in the Southern part of New Zealand found evidence of *Salmonella* infection in two of 60 (3.3%) cases of ReA (Highton and Priest, 1996). However, the total incidence of ReA in New Zealand is unknown. A German study identified *Salmonella* in stool samples of 6% of a case series of 33 cases with 'enteric ReA' (ReA following an episode of gastroenteritis) (Fendler *et al.*, 2001). In this cases series, 33% of enteric ReA cases had a preceding *Salmonella* infection.

Information on the rate of ReA following *Salmonella* infection comes mainly from follow-up studies of *Salmonella* outbreaks (Yu and Thomson, 1994). Estimates vary hugely with figures ranging from 5% (Beltran-Fabregat *et al.*, 2006) to 29% (Dworkin *et al.*, 2001). A Canadian follow-up study of sporadic *Salmonella* typhimurium infections concluded that 6% of all cases were considered to have ReA (Buxton *et al.*, 2002).

Kemmeren *et al*. (2006) assumed that development of ReA was most likely in more serious cases (i.e. those attending a GP) and based their estimate of ReA cases following *Salmonella* infection on 8% (95% CI 2.3-15%) of cases visiting a GP. However, scenarios based on 8% of all *Salmonella*-associated GE cases, and 8% of laboratory-confirmed *Salmonella* cases, were also examined (Kemmeren *et al.*, 2006). In the absence of *Salmonella*-specific data, it was assumed that the pattern of *Salmonella*-linked ReA would be similar to *Campylobacter*-linked ReA and that 22% of cases would attend a GP, while 2.2% would be hospitalised.

The Dutch study also assumed that the duration of *Salmonella*-triggered ReA would be the same as *Campylobacter*-triggered ReA and simulated this variation as an exponential function with a mean of 0.608 years.

The Dutch approach was followed for the current study, with the number of cases of *Salmonella*-associated ReA generated from a Pert distribution (0.023, 0.08, 0.15) multiplied by the number of GP cases of salmonellosis.

The proportions of these cases visiting a GP or hospitalised were calculated from Finnish data (Hannu *et al.*, 2002) as described for reactive arthritis following campylobacteriosis (Appendix 1).

The duration of illness was based on the exponential expression derived for the Dutch study, using the time course of ReA from several studies, and the disability weights were taken from the analysis conducted in the same study (Kemmeren *et al.*, 2006).

Inflammatory Bowel Disease

IBD subsequent to a *Salmonella* infection was treated in exactly the same manner as IBD subsequent to a *Campylobacter* infection.

Model outputs for salmonellosis are summarised in Table 7.

Table 7: Model outputs for salmonellosis

Disease State	Incidence (Cases per year)			YLD	YLL	DALYs	
	Mean	5th percentile	95th percentile			Total	Foodborne
GE, total	**16,800**	**5,800**	**29,800**	**66**	**46**		
GE, no GP	12,400	1,500	24,600				
GE, GP only	4,400	3,500	5,700				
GE, Hospitalisation	159	119	214				
GE, Death	2.4	0.5	4.6				
ReA, total	**365**	**184**	**582**	**27**			
ReA, no GP	288	142	467				
ReA, GP	62	19	122				
ReA, Hospitalisation	16	2	40				
IBD, total	**4**			**47**			
Total				**140**	**46**	**186**	**111**

APPENDIX 3 BACKGROUND INFORMATION LISTERIOSIS (PERINATAL)

Perinatal refers to pregnant women and their fetuses or newborn. Approximately two thirds of pregnant women with *Listeria monocytogenes* infections present with influenza-like symptoms, including fever, chills and headaches (Kemmeren *et al.*, 2006). After 3-7 days the woman may abort the foetus or enter premature labour. Listeriosis is rarely severe or life-threatening for the mother. Neonates may exhibit early-onset or late-onset listerial infections. Early-onset results from infection *in utero* and occurs in neonates less than 7 days old, usual involving sepsis and, in 20% of cases, meningitis. Late-onset listeriosis is acquired during passage through the birth canal or during Caesarian section and is defined as listeriosis in a neonate 8-28 days old. The Dutch study considered that the burden of health outcomes for early- and late-onset cases were unlikely to differ (Kemmeren *et al.*, 2006). Different definitions of the perinatal period are used for different purposes (up to 7 days after birth, up to 28 days after birth). The current study used a definition including infants up to 28 days after birth, to allow inclusion of late onset listeriosis cases.

During the period 1997-2005, 2-9 (mean 5.1) perinatal cases of listeriosis have been notified to the New Zealand national surveillance system (Episurv) each year. Of these cases, 0-6 (mean 2.7) fatalities were reported per annum during the period 1997-2005, giving a mean cases fatality rate in foetuses/infants of 52%. Information obtained from NZHIS does not allow distinction to be made between perinatal and acquired cases. During the same period the number of live births registered in New Zealand have been in the range 54,021-59,193 (http://www.stats.govt.nz/NR/rdonlyres/C491C91A-9F76-4592-99F1-A2EBBDDCB451/0/Births.xls).

Of 46 cases of perinatal listeriosis reported to national surveillance between 1997 and 2005, 24 resulted in death of the foetus or infant, with 22 of the deaths reported as intra-uterine and the remaining two occurring within two days of birth. Of the 22 children surviving perinatal listeriosis or for which outcome was unknown, child illness was reported in 7 cases. Although, it should be noted that there were inconsistencies in reporting of this information.

Mylonakis *et al*. (2002) considered information from over 200 cases of perinatal listeriosis, taken from the international literature. They concluded that spontaneous abortion, stillbirth or early death of a pre-term baby occurred in about 20% of cases. The high mortality rate in New Zealand may be due to the fact that only more serious cases are detected and/or notified, although a New Zealand study carried out in Christchurch during 1981-82 also reported a 50% mortality rate (three spontaneous abortions and one neonatal death amongst eight perinatal listeriosis cases (Faoagali and Schousboe, 1985), while a further New Zealand study reported six deaths (five fetal and one neonatal) from 22 perinatal listeriosis cases (27%) (Lennon *et al.*, 1984).

Overseas studies found that approximately two-thirds of surviving infants developed neonatal listeriosis (Mylonakis *et al.*, 2002), while data from the New Zealand national surveillance system found only one-third of records of perinatal listeriosis cases with a surviving infant contained reference to infant illness. This may be a reporting artifact.

Mylonakis *et al*. (2002) found septicaemia to be the most common clinical sign associated with neonatal listeriosis cases, followed by pneumonia and meningitis. Of 94 neonatal cases , 59 (63%) recovered completely, 23 (25%) died and 12 (13%) suffered neurological or other long-term sequelae.

Enhanced surveillance of *Listeria monocytogenes* infections was carried out in the Netherlands, detecting two cases of pregnancy-related listeriosis during a six-month period. Both cases died. While a range of outcomes are possible following perinatal listeriosis, from death to premature birth of a healthy child, the Dutch disease burden calculation was based solely on the years of life lost (YLL) due to perinatal listeriosis fatalities (Kemmeren *et al.*, 2006).

For the current study, the total number of perinatal cases was taken from New Zealand national surveillance and defined as a pert distribution, with a most likely value equal to the number of cases in 2005 (5) and minima and maxima being the lowest (2) and highest (9) numbers of annual cases notified during the period 1997-2005. The probability of fetal death was defined by a Beta distribution, based on 22 fetal deaths from 46 perinatal listeriosis cases during the period 1997-2005. The number of live births was calculated by difference.

Subsequent outcomes for live births were calculated through a series of beta distributions, based on the study of Mylonakis *et al*. (2002), which summarised data from review of 222 cases of perinatal listeriosis :

- Probability of infection Beta(98, 82)
- Probability of septicaemia Beta(67,32)
- Probability of meningitis Beta(24,75)
- Probability of pneumonia Beta(56,33)
- Probability of death Beta(24,75)
- Probability of long-term sequelae Beta(13,86)

The durations of the various disease states and the associated disability weights were taken from Kemmeren *et al*. (2006), for acquired listeriosis:

- Septicaemia Duration = 0.02 years Disability weight = 0.93
- Meningitis Duration = 0.5 years Disability weight = 0.32
- Pneumonia Duration = 0.02 years Disability weight = 0.04
- Long-term sequelae Duration = 7 years Disability weight = 0.25

Years of life lost due to fetal and neonatal fatalities was taken as the mean life expectancy for males and females less than one year (78.2 years).

Model outputs for perinatal listeriosis are summarized in Table 8.

Table 8: Model outputs for perinatal listeriosis

Disease State	Incidence (Cases per year)			YLD	YLL	DALYs	
	Mean	5th percentile	95th percentile			Total	Foodborne
Septicaemia	1.2	0.7	1.9				
Meningitis	0.4	0.2	0.7				
Pneumonia	1.2	0.6	1.8				
Death - perinatal - neonatal	 2.5 0.4	 1.4 0.2	 3.8 0.7				
Neurological sequelae	0.2	0.1	0.4				
Total				**0.5**	**228**	**229**	**195**

APPENDIX 4 BACKGROUND INFORMATION ACQUIRED LISTERIOSIS

Acquired listeriosis is a relatively rare disease and most healthy individuals do not experience overt symptoms with listerial infection.

Notified cases of acquired listeriosis in New Zealand are in the range 13-26 cases per annum, with 15 cases notified in 2005. Notification of listeriosis cases is quite rigorous with a study of laboratory confirmed cases concluding that 90% (95% CI 56-100%) of laboratory-confirmed cases are notified (Simmons *et al.*, 2002).

A Dutch study concluded that the most common sign of invasive listeriosis was septicaemia (37%), followed by meningitis (22%), gastroenteritis (22%) and pneumonia (15%) (Kemmeren *et al.*, 2006). New Zealand hospital discharge records suggest a different pattern of outcomes in New Zealand. Of 71 patients with listeriosis as the primary diagnosis, discharged between 2000 and 2006 and corrected to exclude readmissions, 55% had listerial meningitis, 30% listerial septicaemia and the remainder (15%) were other or unspecified forms of listeriosis. Of cases with a primary diagnosis of listerial meningitis, 5% had a secondary or tertiary diagnosis of listerial septicaemia. Acquired listeriosis often occurs in patients with an existing serious medical condition. A further 88 discharge records (after correction for readmissions) reported listeriosis in diagnosis codes 2-9, with 22% recorded as listerial meningitis, 23% as listerial septicaemia and 55% as other or unspecified. Only two of the 88 recorded contained more than one listeria diagnosis code (one case with listerial meningitis and septicaemia and one case with listerial septicaemia and other form of listeriosis). When data were combined across all diagnosis codes 36% of cases were diagnosed with listerial meningitis and 26% with listerial septicaemia. It was assumed that the remaining cases (37%) would be equally divided between gastroenteritis and pneumonia cases. The duration of illness and the disability weights were taken directly from the Dutch study (Kemmeren *et al.*, 2006).

A further Dutch study demonstrated that 14% of adults who developed listerial meningitis would develop neurological sequelae (Aouaj *et al.*, 2002). This proportion and the associated duration and disability weights were taken from the Dutch study and applied to the current study (Kemmeren *et al.*, 2006).

The case fatality rate for cases with sepsis, meningitis or gastroenteritis has been reported to be 18% (Kemmeren *et al.*, 2006). Data from national surveillance in New Zealand indicates mortality rates for notified listeriosis cases of 20.8%. However, the majority of these deaths were due to underlying conditions and examination of case records indicated that death due to listeriosis in New Zealand was in the range 0-13% (mean = 7.3%) of notifications per annum. The number of fatal acquired listeriosis cases in New Zealand was calculated from the total number of cases using observed cases fatality rates, modeled as a Pert distribution with most likely value 0.073, minimum of zero and maximum of 0.13. A distribution was fitted to the ages of all reported listeriosis fatalities in New Zealand (1997-2005) and values were drawn from this distribution and combined with life expectancy tables for New Zealand to estimate the number of years of life lost.

Model outputs for acquired listeriosis are summarised in Table 9.

Table 9: Model outputs for acquired listeriosis

Disease State	Incidence (Cases per year)			YLD	YLL	DALYs	
	Mean	5th percentile	95th percentile			Total	Foodborne
Listeriosis (Acquired)							
Sepsis	4.9	3.4	6.7				
Meningitis	7.5	5.5	10.1				
Gastroenteritis	3.6	2.4	5.1				
Pneumonia	3.6	2.4	5.1				
Death	1.4	0.5	2.3				
Neurological sequelae	1.0	0.8	1.4				
Total				**5**	**21**	**26**	**22**

APPENDIX 5 BACKGROUND INFORMATION STEC INFECTION

STEC infection may be asymptomatic or may result in diarrhoea and, potentially, haemorrhagic colitis. Initial infection may result in bloody diarrhoea, non-bloody diarrhoea or asymptomatic infection. STEC infection has also been associated with post-diarrhoeal haemolytic uraemic syndrome (HUS). HUS occurs mainly in young children and may result in death, end stage renal disease (ESRD) or other sequelae (Havelaar *et al.*, 2004). Acute renal failure is the most prominent feature of HUS and can lead directly to ESRD or renal damage may become apparent after a period of normal kidney function (Havelaar *et al.*, 2004).

Acute gastroenteritis

The notified incidence of STEC infection in New Zealand is currently about 100 cases per annum (92 cases in 2005, range 67-105 since 2000). Simmons *et al*. (2002) reported that 100% (95% CI 48-100%) of laboratory-confirmed STEC/VTEC cases in New Zealand were notified.

An overseas review of 10 STEC (*E. coli* O157) outbreaks found 253/568 (44.5%) of cases had bloody diarrhoea (Michel *et al.*, 2000). An investigation of a waterborne outbreak of STEC infection found that 40/55 (73%) of cases with bloody diarrhoea reported to the medical authorities, while only 11/50 (22%) of those with non-bloody diarrhoea reported (Michel *et al.*, 2000).

The New Zealand study of Sarfati *et al*. (1997) found that GPs were more likely to submit stool samples for testing if there was blood in the stool and if the patient was less than five years of age. Of 122 qualifying responses, 95 (78%) reported they would always/often submit a stool sample for testing if blood was present in the stool.

Combining the data above in a simulation, it was estimated that laboratory confirmed cases would be made up of 86% bloody diarrhoea cases and 14% non-bloody diarrhoea. Combining these estimates with the reporting data from Michel *et al*. (2000) allows an estimate to be made of the total number of STEC cases in the community of approximately 320 cases per annum. This is slightly higher than previous estimates for New Zealand of 200-250 cases per annum (Baker *et al.*, 1999; Lake *et al.*, 2000).

Bloody diarrhoea has been reported to have a longer duration than non-bloody and the Dutch study used figures of median 5 days (range 2-12 days) and median 3 days (range 1-7 days) for bloody and non-bloody diarrhoea due to STEC, respectively (Havelaar *et al.*, 2004). For the current study, these figures were used as the basis for Pert distributions.

Non-HUS STEC associated mortality is rare. In the well-documented Walkerton outbreak there was one fatality among 2321 cases (0.04%). There have been no fatalities linked to STEC infection in New Zealand since 1998, with 2 deaths from 627 notified cases since 1997 (0.3%). The New Zealand data were used to define a beta distribution for the proportion of fatal cases. As the two reported fatalities represented quite different scenarios (ages 1 and 72 years). The years of life lost was modeled by giving these two ages equal weights.

HUS

An incidence for HUS of 2.0/100,000 children less than five years has been reported for the Netherlands, with an attributable proportion of 77% for STEC infection (Havelaar *et al.*, 2004). The incidence of HUS in New Zealanders <15 years is 0.9/100,000 (NZPSU, 2005), while the incidence of HUS in New Zealand children under five years has been reported to be 3.9 per 100,000 (Baker *et al.*, 1999). During the 2005 year, five cases of HUS were reported to the New Zealand Paediatric Surveillance Unit, for which an *E. coli* O157 isolation was made from a stool sample (NZPSU, 2005). All cases were less than five years of age. This compared to three cases of HUS, with *E. coli* O157 isolation in 2004. STEC isolation from HUS cases was not reported for earlier years. Given that there are approximately 220,000 New Zealanders less than five years of age and assuming an incidence similar to the Netherlands (2.0/100,000), 3-4 cases of STEC-associated HUS would be expected per annum. This is consistent with observed data from 2004 and 2005, and the Dutch approach was adopted for the modeling of HUS due to STEC infection. Havelaar *et al*. (2004) reported age specific probabilities of developing HUS following STEC-associated gastroenteritis. These probabilities were applied to the observed age distribution of STEC cases in New Zealand to produce an estimate of STEC-associated HUS for New Zealand.

Havelaar *et al*. (2004) reported that, in the Netherlands, for every HUS case in the age range 5-14 years, 8.2 cases would be expected in the 0-4 age group. Analysis of data on hospitalised HUS cases in New Zealand during the years 2001-2006, from hospital discharge records, showed a lower ratio with 57 recorded cases in the 0-4 years range and 14 recorded cases in the 5-14 years range (ratio 4.1).

Havelaar *et al*. (2004) used a case fatality rate for HUS of 32/867 (3.7%) for cases up to 65 years and estimated a case fatality rate for older cases of 56%. Mortality data obtained from the New Zealand Health Information Service does not include any deaths identified to HUS (ICD 10 code D59.3) during the period 2000-2004. However, deaths due to HUS could well have been recorded under ESRD (ICD 10 code N18.0). The approach of Havelaar *et al*. (2004) was used in the current study. Age specific fatality rates were combined with New Zealand life expectancy data to estimate the years of life lost.

ESRD

Havelaar *et al*. (2004) estimated the probability of a HUS case developing direct ESRD (direct outcome of HUS, without recovery of renal function) as 23/734 (2.9%). Late ESRD (following initial recovery of renal function) was estimated to have a probability of 8/76 (10.5%), with onset being uniformly distributed between 0 and 40 years after HUS. The approach of Havelaar *et al*. (2004) was used to model the subsequent duration, disability weights and mortality associated with dialysis, renal transplantation and subsequent graft rejection.

Model outputs for STEC infection are summarised in Table 10.

Table 10: Model outputs for STEC infection

Disease State	Incidence (Cases per year)			YLD	YLL	DALYs	
	Mean	5th percentile	95th percentile			Total	Foodborne
STEC infection							
GE, total	**340**	**180**	**620**	**1.0**	**33**		
GE, bloody	148	96	202				
GE, non-bloody	192	15	505				
GE, death	0.7	0.2	1.5				
HUS, total				**0.5**	**26**		
HUS, clinical	9.3	4.9	16.9				
HUS, death	0.4	0.2	0.8				
ESRD	**1.2**	**0.6**	**2.2**	**16.6**	**14**		
Total				**18**	**73**	**91**	**35**

APPENDIX 6 BACKGROUND INFORMATION YERSINIOSIS

Yersinia enterocolitica infection usually results in simple enteritis. However, in some cases sequelae including reactive arthritis, septicaemia, lymphadenitis, disturbed liver function, and erythema nodosum. The current exercise has only modelled gastroenteritis and reactive arthritis.

Acute gastroenteritis

Notified cases of yersiniosis in New Zealand have been reasonably steady over a long period of time, with 407 cases in the most recent reported year (2005) and total cases ranging between 396 and 546 since 1997. Simmons *et al.* (2002) estimated that 79% (95% CI 72-85%) of laboratory confirmed cases in New Zealand were notified. The symptoms associated with yersiniosis do not suggest that cases will result in requests for stool sample by GPs any more often than any other acute gastrointestinal disease (Sarfati *et al.*, 1997). The approach taken for *Campylobacter* and *Salmonella* was used to estimate the number of yersiniosis cases attending a GP in New Zealand.

A British study produced data suggesting that yersiniosis cases are less likely to present to a GP than sufferers of many other acute gastrointestinal diseases, with 11.7 (95% CI 7.5-18.3) community cases for every GP case, compared to 2.1 for campylobacteriosis and 1.4 for salmonellosis (Wheeler *et al.*, 1999). However, some caution should be attached to this figure, as a Dutch case-control study found *Yersinia* spp. as frequently in controls as in cases, suggesting that asymptomatic carriage is not uncommon (De Wit *et al.*, 2001a). Similarly, the Dutch SENSOR study, a prospective population-based cohort study on gastroenteritis, found *Yersinia* spp. in the stool of controls at twice the rate that the organism was found in the stools of cases (de Wit *et al.*, 2001b) and the British IID study found *Yersinia* as frequently in the stools of controls as cases (Tompkins *et al.*, 1999). For the current study the ratio of total community to GP cases reported by Wheeler *et al.* (1999) was applied. However, based on the evidence outlined above, it was assumed that half of the community cases (not attending a GP) would be asymptomatic and were not included in further calculations.

Yersiniosis is characterised by its extended duration. In a Norwegian case-control study, 48/66 laboratory-confirmed cases had been symptomatic for a mean of 20.0 days (range 1-119 days) (Ostroff *et al.*, 1992). Of the remaining 18 cases, 15 were reinterviewed at one year, at which time six reported continuing symptoms and reported the illness had lasted an average of 39.0 days (range 28-65). A study of pediatric cases in the US found a similar duration of illness (Lee *et al.*, 1991). Of the 38 cases investigated, the median duration of illness was greater than 10 days (range 5-30). Fourteen cases were hospitalised for a median of 3.5 days (range 2-12).

No information was located on the duration of illness for community (non-GP visit) cases. It was assumed that for these cases the duration would be similar to those reported for campylobacteriosis and salmonellosis, and the mean of the values previous used for these diseases in this study was applied.

Hospitalisations due to yersiniosis have varied in the range 17-41 per annum, as reported by national surveillance. Figures from hospital discharge data gives lower numbers; 7-17 based on the primary diagnosis code and 18-31 based on any diagnosis code. The number of

hospitalised cases was modeled as a Pert distribution with most likely value of 41 (the figure for 2005), with a minimum of 17 and a maximum of 41.

Fatalities due to yersiniosis are reasonably rare, with only three fatalities identified through the national surveillance system (Episurv) since 1997 and none identified through national mortality records during the period 2001-2004. The number of fatalities was modeled as a pert distribution with the most likely value being the mean for the years 1997-2005 (0.33), the minimum equal to zero and a maximum of two. The ages of the three reported fatalities were used to define a Pert distribution for the age at death, which was combined with New Zealand life expectancy data to estimate the years of life lost.

Reactive Arthritis

A study carried out in the Southern part of New Zealand found evidence of *Yersinia enterocolitica* infection in eight of 60 (13.3%) cases of ReA (Highton and Priest, 1996). However, the total incidence of ReA in New Zealand is unknown. A German study identified *Yersinia* in stool samples of 3% of a case series of 33 cases with 'enteric ReA' (ReA following an episode of gastroenteritis) (Fendler *et al.*, 2001). In this cases series, 18% of enteric ReA cases had a preceding *Yersinia* infection.

A retrospective study in Auvergne, France identified 42 cases of *Yersinia* infection (Gourdon *et al.*, 1999). Six cases (14%) were reported as having 'arthritis'. However, there was no indication whether these cases met the case definition for ReA. A Dutch case series of 261 cases with *Yersinia* infection only reported 15 cases (6%) with subsequent arthritis (Stolk-Engelaar and Hoogkamp-Korstanje, 1996). This figure was used to model the proportion of yersiniosis cases developing ReA, subsequent to infection (beta distribution, alpha = 16, beta = 247).

Kemmeren *et al*. (2006) assumed that development of ReA was most likely in more serious cases (i.e. those attending a GP) and based their estimate of ReA cases following *Salmonella* infection on 8% (95% CI 2.3-15%) of cases visiting a GP, while for ReA following *Campylobacter* infection a figure of 7% was used. The same approach was used in the current study, with ReA cases being calculated as a proportion of yersiniosis cases attending a GP.

Kemmeren *et al*. (2006) assumed that the duration of bacteria triggered ReA would be the same, no matter which organism triggered the condition, and simulated this variation as an exponential function with a mean of 0.608 years.

Model outputs for yersiniosis are summarised in Table 11.

Table 11: Model outputs for yersiniosis

Disease State	Incidence (Cases per year)			YLD	YLL	DALYs	
	Mean	5th percentile	95th percentile			Total	Foodborne
Yersiniosis							
GE, total	**7,900**	**5,700**	**10,400**	**57**	**29**		
GE, no GP	6,600	4,500	9,000				

Disease State	Incidence (Cases per year)			YLD	YLL	DALYs	
	Mean	5th percentile	95th percentile			Total	Foodborne
GE, GP only	1,300	1,200	1,450				
GE, Hospitalisation	37	30	41				
GE, Death	0.5	0.1	1.2				
ReA, total	**80**	**50**	**115**	**7**			
ReA, no GP	63	38	92				
ReA, GP	14	5	25				
ReA, Hospitalisation	3	1	8				
Total				**64**	**29**	**93**	**52**

APPENDIX 7 BACKGROUND INFORMATION NOROVIRUS INFECTION

Acute gastroenteritis is assumed to be the only condition relevant to norovirus (NV) infection (Kemmeren *et al.*, 2006). No systematic information is available on the number of annual norovirus cases in New Zealand. Lake *et al*. (2000) extrapolated from the results of a UK study (Wheeler *et al.*, 1999) to estimate 46,000 community cases of NV infection per annum, including 7,300 GP visits. For the Netherlands, with a population of approximately 16 million, an estimate of 472,000 NV cases per annum, with 11,000 GP visits was made (Kemmeren *et al.*, 2006). Pro-rata of these figures to the New Zealand population gives a higher number of cases (118,000) and a lower number of GP visits (2,750) than the estimate of Lake *et al*. (2000). Australia, with a population of approximately 20 million, has been estimated to have approximately 1.8 million NV cases per annum, which would pro rata to approximately 360,000 cases per annum in New Zealand (Hall and Kirk, 2005).

Norovirus infection is not a notifiable disease in New Zealand. However, since July 2000, Public Health Services in New Zealand have been encouraged to record all cases of gastroenteritis caused by non-notifiable or unknown food-borne intoxicants including those self-reported by the public. A causal organism is reported for a proportion of these cases, with norovirus being the most commonly reported organism, with 14-198 norovirus cases reported through this channel each year. An analogous situation exists in England with cases of 'food poisoning' required to be notified, in addition to notifications for specified infectious diseases (Food Standards Agency, 2000). 'Food poisoning' is defined as 'any disease of an infectious or toxic nature caused or thought to be caused by the consumption of food or water'. While this is not exactly the same as the New Zealand notification category 'acute gastroenteritis', it is similar and both provide a mechanism whereby norovirus cases come to the attention of the notification system. As part of the English IID study, Wheeler *et al*. (1999) estimated that for every NV case reported to national surveillance 1562 (95% CI 140-17,424) community cases occurred, of which 248 (95% CI 30.4-2026) would attend a GP. The number of notified NV cases for New Zealand and the under-reporting factors determined for England were used to estimate the total number of NV cases in New Zealand. Pert distributions were used to model the number of notified NV cases and the under-reporting factors for total and GP cases. Using this approach the mean total number of NV cases for New Zealand is 128,700.

According to hospital discharge data (primary diagnosis code only), 7-34 cases per annum are hospitalised due to NV infections. These figures are very similar to figures published for Australia (mean = 17, range = 2-32) (Hall and Kirk, 2005). The Dutch study modeled the hospitalisation due to NV as 0.33% of cases. Using this proportion to calculate total cases, based on hospitalisations, gives a total number of NV cases for New Zealand in the range 2000-10,000.

The Dutch burden of illness study used duration figures of 3.8 days for community cases, 5.73 days for cases attending a GP, but not hospitalised and 7.23 days for hospitalised cases (Kemmeren *et al.*, 2006). Analysis of New Zealand hospital discharge data gave an average length of stay for patients admitted with a primary diagnosis code of A08.1 (acute gastroenteropathy due to Norwalk agent) of 3.8 days.

Model outputs for norovirus infection are summarised in Table 12.

Table 12: Model outputs for norovirus infection.

Disease State	Incidence (Cases per year)			YLD	YLL	DALYs	
	Mean	5th percentile	95th percentile			Total	Foodborne
Norovirus infection							
GE, total	**403,000**	**71,000**	**1,004,000**	**530**	**6**		
GE, no GP	357,000	43,000	942,000				
GE, GP only	46,000	7,000	116,000				
GE, Hospitalisation	18	10	27				
GE, Death	0.8	0.2	1.4				
Total				**530**	**6**	**536**	**210**

APPENDIX 8 ICD CODES FOR REQUEST TO NZHIS

The following codes were the subject of the information requested from NZHIS.

Module	Disease type	Disease	Code	Description
Campylobacter	Direct	Gastroenteritis	A04.5	Campylobacter enteritis
Campylobacter	Indirect	Guillain-Barre Syndrome	G61.0	Guillain-Barre Syndrome (GBS)
Campylobacter	Indirect	Reactive Arthritis	M02.1	Postdysenteric arthropathies
Campylobacter	Indirect	Reactive Arthritis	M02.3	Reiter's disease
Campylobacter	Indirect	Reactive Arthritis	M02.8	Other reactive arthropathies
Campylobacter	Indirect	Reactive Arthritis	M02.9	Reactive arthropathy, unspecified
Campylobacter	Indirect	Reactive Arthritis	M46.9	Inflammatory spondylopathy, unspecified
Campylobacter	Indirect	Inflammatory Bowel Disease	K50	Crohn's disease
Campylobacter	Indirect	Inflammatory Bowel Disease	K51	Ulcerative colitis
Salmonella	Direct	Gastroenteritis	A02	Other salmonella infections
Salmonella	Direct	Gastroenteritis	A02.0	Salmonella enteritis
Salmonella	Direct	Gastroenteritis	A02.1	Salmonella septicaemia
Salmonella	Direct	Gastroenteritis	A02.8	Other specified salmonella infections
Salmonella	Direct	Gastroenteritis	A02.9	Salmonella infection, unspecified
Salmonella	Indirect	Reactive Arthritis		As for Campylobacter
Salmonella	Indirect	Inflammatory Bowel Disease		As for Campylobacter
Listeria	Direct	Listeriosis	A32	Listeriosis (excluding Neonatal (disseminated) listeriosis)
Listeria	Direct	Listeriosis	A32.1	Listerial meningitis and meningoencephalitis
Listeria	Direct	Listeriosis	A32.7	Listerial septicaemia
Listeria	Direct	Listeriosis	A32.8	Other forms of listeriosis
Listeria	Direct	Listeriosis	A32.9	Listeriosis, unspecified
Listeria	Direct	Listeriosis	P37.2	Neonatal (disseminated) listeriosis
STEC	Direct	Gastroenteritis	A04.3	Enterohaemorrhagic Escherichia coli infection
STEC	Direct	Gastroenteritis	A04.0	Enteropathogenic Escherichia coli infection
STEC	Direct	Gastroenteritis	A04.1	Enterotoxigenic Escherichia coli infection
STEC	Direct	Gastroenteritis	A04.2	Enteroinvasive Escherichia coli infection
STEC	Direct	Gastroenteritis	A04.4	Other intestinal Escherichia coli infections
STEC	Indirect	HUS	D59.3	Haemolytic uraemic syndrome
STEC	Indirect	ESRD	N18.0	End stage renal disease
Yersinia	Direct	Gastroenteritis	A04.6	Enteritis due to Yersinia enterocolitica (excluding extraintestinal yersiniosis)
Yersinia	Indirect	Reactive Arthritis		As for Campylobacter
Yersinia	Indirect	Erythema nodosum	L52	Erythema nodosum
Norovirus	Direct	Gastroenteritis	A08.1	Acute gastroenteropathy due to Norwalk agent