A systematic review of the human disease evidence associated with the consumption of raw milk and raw milk cheeses

A report prepared for the New Zealand Food Safety Authority (NZFSA) by

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Contents

Executive summary

The New Zealand Food Safety Authority (NZFSA) is proposing a framework that would allow a wider variety of raw milk products to be sold and produced in New Zealand. Under the proposed framework raw milk products would be categorised according to the risks they present. To inform the standard setting process, and aid the development of a risk communication strategy, a systematic assessment of the available morbidity and mortality evidence associated with consumption of raw milk and raw milk cheese was required.

The objective of the review was to identify primary studies describing human diseases associated with the consumption of unpasteurised dairy products, and to evaluate evidence presented in these studies. The review focused on publications reporting food poisoning linked to raw milk, raw milk cheeses (e.g. Mexican-style cheeses, Roquefort), and other untreated products and by-products of raw milk (e.g. cream, raw milk butter, fermented products, yoghurt, butter milk, and whey) of bovine, goat, sheep, or buffalo origin, contaminated with pathogens such as *Bacillus cereus*, *Brucella* spp., *Campylobacter* spp., *Coxiella burnetii*, *E.coli* spp., *Listeria monocytogenes*, *Mycobacterium bovis*, *Salmonella* serovars, *Shigella* spp., *Staphylococcus aureus*, *Streptococcus* spp., *Yersinia* spp., and *Toxoplasma* spp.

The review process began with the systematic retrieval of relevant studies, which involved computerised search via published databases, hand searching, discussion with relevant experts and internet sources, to retrieve both published and unpublished work up to early August 2008. Studies were then categorised as either 'Type 1'[1] or 'Type 2'[2] studies. Only Type 1 studies were evaluated for internal validity. If the score for internal validity was greater than or equal to 25, then the paper was considered to have adequate internal validity to assess causality, and was entered into the next stage of the review process: scoring causality and relevance. The evidence of a causal link between the pathogen and consumption of raw milk and/or raw milk products was considered separately for each of the pathogens. The first step was to determine, for each pathogen, the number of Type 1 studies with adequate internal validity (i.e. interval validity score ≥ 25). We considered there to be insufficient evidence to objectively evaluate, if there was a causal link between consumption of raw milk and

[1] 'Type 1' studies were those studies that include both exposed and non-exposed individuals (i.e. cohort, case-control, cross-sectional studies) and outbreak investigations that provided information about the total number of individuals exposed.

[2] 'Type 2' studies included outbreak investigations (without denominator data), surveys, case reports, and case series.

infection with a particular pathogen if less than four Type 1 studies with adequate internal validity were available. Summary measures of causality and relevance were calculated for all agents with greater than or equal to four Type 1 studies with adequate internal validity.

Database searches identified a total of 272 articles with evidence of adverse health effect(s) in humans after consumption of contaminated unpasteurised dairy products. Of these, only 84 were considered to provide reasonable data for assessment in the systematic review (i.e. classified as Type 1 studies). Raw milk was reported as the most likely vehicle of infection in 52% (44/84 articles) of incidences, whereas unpasteurised cheese was involved in 23% (19/84 articles). In 83% (70/84 articles) of studies, dairy product(s) of bovine origin were identified as the source of infection. The largest number of studies was related to bacterial infections of *Campylobacter* spp. (27/84 articles), followed by *Salmonella* serovars (10/84 articles) and *Listeria monocytogenes* (9/84 articles).

Based on the evidence collected, it was not possible to demonstrate a strong causal link between consumption of raw milk or dairy products made from raw milk and any of the pathogens considered in this review. The evidence examined in this review did provide moderate evidence to support a causal link between consumption of raw milk/raw milk products and the following pathogens:

- *Campylobacter* spp.;
- *E. coli* spp.;
- *Listeria monocytogenes*; and
- *Salmonella* serovars.

There was also some evidence, albeit weak, to support a causal link between infection with *Brucella* and the consumption of raw milk products. Owing to the shortage of studies and/or shortage of studies with adequate internal validity, it was not possible to objectively evaluate if there was a causal link between exposure to raw milk and products made from raw milk and the infections caused by the following:

- *Coxiella burnetii*,
- *Mycobacterium bovis*,
- *Shigella* spp.,
- *Staphylococcus* spp.,
- *Streptococcus* spp.,
- *Yersinia* spp.,
- *Cryptosporidium* spp.,

and the conditions Crohn's disease and cancer.

A meta-analysis was not conducted as part of this review; however, the available literature was evaluated to determine whether there was sufficient information to be included in a meta-analysis. Based on our findings the lack of well designed studies precluded the use of a meta-analysis to assess the available evidence.

List of Figures

List of Tables

1 Introduction

1.1 Systematic review

A systematic review is a summary of (all) the available primary research identified on a particular topic which is analysed in a systematic manner. A standardised method is used to assess the internal and external validity of research findings. Systematic reviews are constructed in a pre-planned and documented way to allow repeatability as well as its critical appraisal. In contrast, traditional literature reviews are a description of previous work without systematically identifying and assessing its quality. In general, systematic reviews aim to illustrate consistency (or deviation) of study results but also identify existing gaps of knowledge; they are useful tools in decision-making processes and developments of policies or standards where unbiased scientific information is required.

1.2 Background and rationale

The New Zealand Food Safety Authority (NZFSA) is proposing a framework that would allow a wider variety of raw milk products to be sold and produced in New Zealand. Under the proposed framework raw milk products would be categorised according to the risks they present. The organisation has completed a quantitative risk assessment estimating the risk to New Zealand consumers from the consumption of raw milk[3] and raw milk cheeses[4]. To inform the standard setting process and aid the development of a risk communication strategy, a systematic analysis of the available morbidity and mortality evidence associated with consumption of raw milk and raw milk cheese is required. Although previous literature reviews have described the studies relating the risks to consumers from the consumption of raw milk and raw milk cheeses, none of these reviews have evaluated the quality of the existing information in a systematic manner.

The objective of the present systematic review was to analyse primary studies describing the morbidity and mortality associated with the consumption of raw milk and raw milk cheeses and to evaluate the internal and external quality of the data. In addition, the review aimed to determine whether the data are of sufficient quality to warrant a meta-analysis.

[3] In this report raw milk is defined as untreated milk that has not been heated (pasteurised).
[4] Cheeses made from raw milk are referred to as raw milk cheeses.

2 Materials and Methods

2.1 Scope of the review

A workshop at the beginning for the project limited the scope of the systematic review to literature reporting human disease incidences associated with the consumption of raw milk and raw milk cheeses. Discussions during the workshop indicated that the review should focus on publications reporting food poisoning linked to raw milk, raw milk cheeses (e.g. Mexican-style cheeses, Roquefort), and other untreated products and by-products of raw milk (e.g. cream, raw milk butter, fermented products, yoghurt, butter milk, and whey) of bovine, goat, sheep, or buffalo origin as possible causes of human diseases. Ice cream made from raw milk was not considered in this systematic review. A report on the workshop can be found in Appendix VI of this report.

Pathogens considered in this systematic review causing adverse health event(s) due to consumption of raw milk or raw milk products are described in Table 1.

Table 1: Major pathogens (*in italics*) and related human diseases.

Pathogen type	Pathogen name	Disease
Bacterium	*Bacillus cereus*	Bacillosis
	Brucella spp.	Brucellosis
	Campylobacter spp.	Campylobacteriosis
	Coxiella burnetii	Q fever
	E.coli spp.	Enteritis, Haemolytic Uraemic Syndrome (HUS)
	Listeria monocytogenes	Listeriosis
	Mycobacterium bovis	Tuberculosis
	Salmonella serovars	Salmonellosis
	Shigella spp.	Shigellosis
	Staphylococcus aureus	*Staphylococcus* infection
	Streptococcus spp.	*Streptococcus* infection
	Yersinia spp.	Yersiniosis
Parasite	*Toxoplasma*	Toxoplasmosis

2.2 Overview of the systematic review process

The systematic review involved a number of steps including searching and retrieval of papers and scoring of the articles. Figure 1 provides a schematic representation of this process.

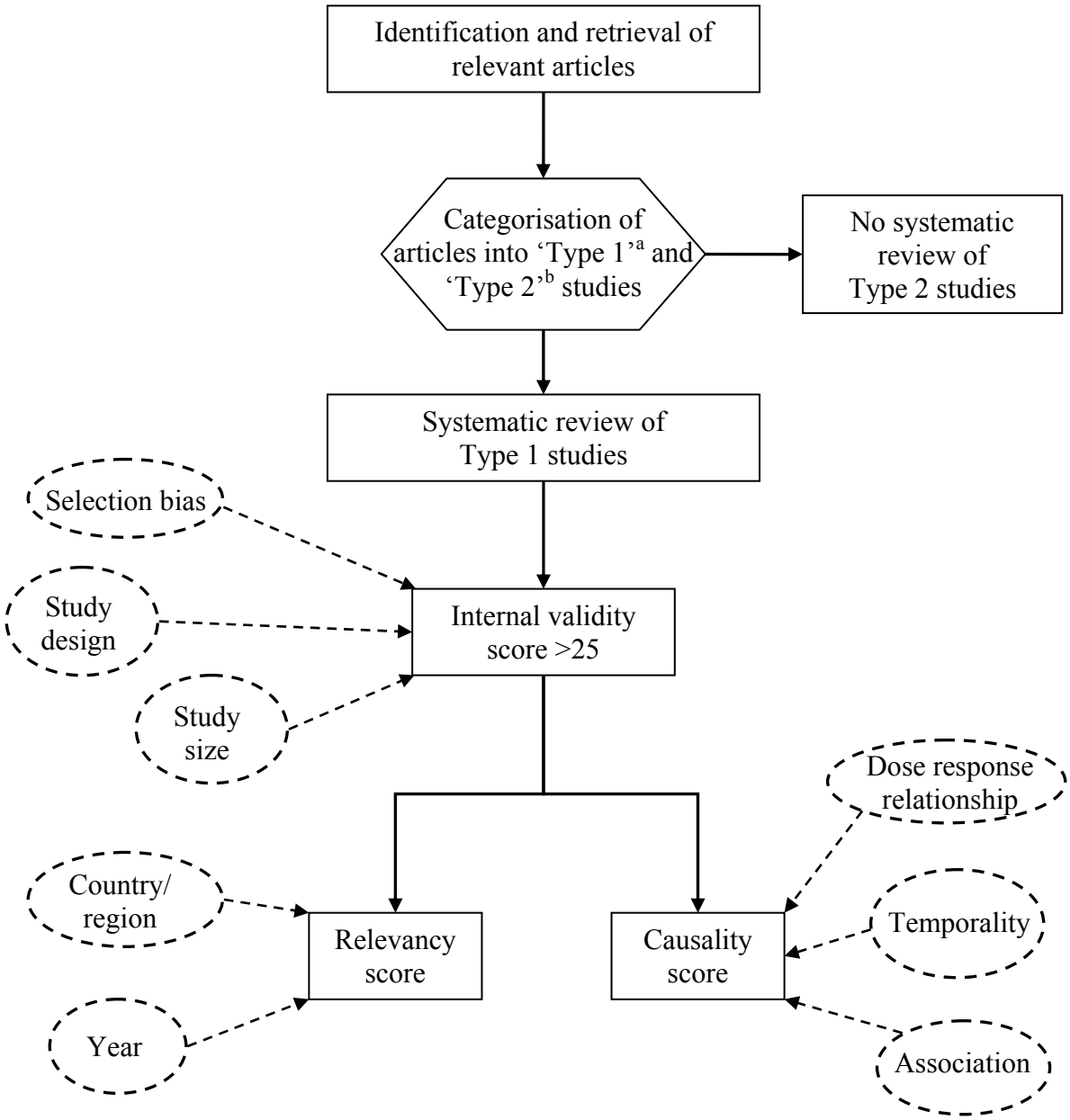

Figure 1: Overview of method used to complete a systematic review of studies related to raw milk/cheese consumption and adverse health effects in humans.
[a] 'Type 1' studies are randomised control trials, cohort, case-control, cross-sectional studies, and outbreak investigations with denominator.
[b] 'Type 2' studies are comprised of outbreak investigations (without a denominator), surveys, case reports, and case series.

2.3 Identification and retrieval of relevant studies

Systematic retrieval of relevant studies involved computerised search via published databases, hand searching, discussion with relevant experts and internet sources to retrieve both published an unpublished work up to early August 2008. The search of electronic databases included Web of Knowledge[5] (1990-2008), ScienceDirect[6] (1823-2008) and PubMed- via Medline[7] (1950-2008). The search methods used allowed retrieval of all types of study design, including descriptive (surveys, reports and outbreak investigations) and observational studies (experiment, cohort, case-control, and cross-sectional studies) without any restrictions applied on year of publication, country of study or language of paper. There was, however, some variation between the databases in the keywords. Table 2 provides an example of the keyword search for *Campylobacter* associated articles. When searching for articles related to other causal pathogen/human disease, the term *campylobact** was replaced by one of the terms in Table 3. Only papers with an English language abstract were retrieved for classification (see Section 2.4).

Google Scholar[8], websites of food safety authorities of the UK, USA, Canada, Ireland, Australia, the European Union; and websites of public health and food agencies of Denmark and the Netherlands were also searched for related reports. In Google Scholar, the search term *(milk raw OR unpasteurised OR outbreak OR epidemic –incidence –occurrence –PCR –effect)* was used with no restrictions imposed other than to seek for words within the title. All articles of Medicine, Pharmacology, and Veterinary Science classification were searched. Newspaper articles or stories published on the web were not considered.

Reference lists of relevant articles were also scanned to identify further articles that may have been missed by the electronic database search, and selected if thought to be relevant for further examination.

For all searches done using electronic databases and Google Scholar, the number records retrieved and the number that were considered relevant was recorded. Details of all articles to be considered further were entered into a customised Microsoft Access database. Percentage accuracy was calculated for each electronic database and Google Scholar. The percentage accuracy is a measurement based on the number of relevant and retrieved articles of each

[5] Web of Knowledge is an article database that allows the user to simultaneously search the article databases Web of Science, Current Contents Connect®, ISI Proceedings, CAB Abstracts®, and Web Citation Index™.
[6] ScienceDirect searches within Elsevier journals, books and reference works only.
[7] PubMed searches within MEDLINE and other life science journals for biomedical articles back to the 1950s.
[8] Google scholar provides access to peer-reviewed papers, theses, books, abstracts and articles.

search engine used and was calculated by dividing the number of relevant articles by the total number of articles retrieved (returns) and multiplied by 100.

Table 2: Keywords used to search for articles associated with *Campylobacter* for each of the electronic databases used to retrieve articles.

Database	Product	Keywords
Web of Knowledge	Milk	*((raw or unprocessed or untreated or unpasteur*) milk* (diseas* or "public health" or epidemi* or infec* or fatal*) campylobact*)*
	Cheese	*((raw or unprocessed or untreated or unpasteur*) cheese* (diseas* or "public health" or epidemi* or infec* or fatal*) campylobact*)*
ScienceDirect	Cheese and milk	*((raw or unprocessed or untreated or unpasteur*) AND (milk* or cheese*) AND (diseas* or "public health" or epidemi* or infec* or fatal* or outbreak) AND campylobact*)* (e.g. for *Campylobacter* spp.).
PubMed	Cheese and milk	*((raw or unprocessed or untreated or unpasteur*) AND (milk* or cheese*) AND (diseas* or "public health" or epidemi* or infec* or fatal*) AND campylobact*)* (e.g. for *Campylobacter* spp.).

Table 3: Keywords used for pathogens or human diseases in electronic article database searches.

Pathogen name or human disease	Keyword used
Campylobacter spp.	campylobact*[a]
Salmonella serovars	salmonell*
E.coli spp.	E.coli*
Listeria monocytogenes	Listeri*
Tuberculosis	Tubercul*
Bacillus cereus	Bacill*
Brucella spp.	Brucell*
Streptococcus spp.	Streptococc*
Yersinia spp.	Yersini*
Staphylococcus aureus	Staphylo*
Shigella spp.	Shigell*
Q fever	Q fever
Toxoplasma	Toxoplasm*

[a] * represents a wildcard symbol which will find words with the same stem.

2.4 Screening of publications

All articles in the Microsoft Access database were screened in a two step process: (i) Categorisation into 'Type 1' and 'Type 2' and (ii) Scoring internal validity of 'Type 1' studies. When the English abstract/summary for a paper written in another language suggested that the paper may have valuable information in the summary, project personnel translated the paper. In the case of papers written in French and German the translation was done by one of the study personal (PJ). For papers written in other languages the translation was done using international staff within the EpiCentre. Only studies classified as 'Type 1' were considered further in the systematic review.

Categorisation of studies into the two study types was based on study design (Table 4). 'Type 1' studies were those studies that include both exposed and non-exposed individuals (i.e. cohort, case-control, cross-sectional studies) and outbreak[9] investigations that provided information about the total number of individuals exposed. In contrast, 'Type 2' studies only contained information about the cases. 'Type 2' studies included outbreak investigations (without denominator data), surveys, case reports, and case series. While Type 2 studies suggest that raw milk and raw milk products may cause disease, they provide insufficient data to assess causality as such and were not considered further in this systematic review.

The next step was to evaluate the internal validity of Type 1 studies. The score was generated by assessing (i) study design, (ii) study size, and (iii) measures applied to minimise study bias due to misclassification of disease and exposure status, confounding and selection bias (due to low response rates). Table 5 describes the semi-quantitative ranking system used to score each of the criteria. The internal validity score for each article was then determined by summing the scores for each of the six criteria. The internal validity score for an article was between four and 53. Studies with internal validity scores of less than 25 were not considered to have adequate internal validity for investigating causal relationships and were not considered further. In contrast, Type 1 studies with score greater than or equal to 25 were considered to have adequate internal validity to assess causality and were entered into the next stage of the review process, scoring causality and relevance.

[9] An outbreak is defined as two or more related cases of illness (linked to the same source of infection, a common food).

Table 4: Definition and strength of causal evidence that can be demonstrated by the study for each of the study types identified in the systematic review.

Study type	Definition/example	Strength to show causal association[a]
Type 1		
Experiment	Human volunteers drink milk sample with known dose of pathogen; investigator observes and takes samples during disease development	Very high
Cohort	Measuring the occurrence of particular disease in specified groups which either consume or do not consume contaminated dairy products over a set period of time	High
Case-control	Contrasting dietary history of patients (cases) with non-affected controls to identify dietary risk factor(s) such as contaminated dairy product(s)	Moderate
Cross-sectional	Selected groups are examined for their health status of a particular disease and interviewed about their consumption of dairy products at the same time	Low
Outbreak investigation with denominator	Investigating an outbreak of food poisoning in order to identify contaminated dairy product(s) as the source of infection; total number of exposed and non-exposed subjects (both ill or healthy) is known	Low
Type 2		
Outbreak investigation without denominator	Investigating an outbreak of food poisoning to identify contaminated dairy product(s); only number of exposed subjects (ill or healthy) is given	NA[b]
Survey	Providing data about frequency/distribution of cases with disease of interest in a defined population	NA
Case series	Describing a series of cases with disease of interest (might provide hypothesis of causal dairy product)	NA
Case reports	Reporting an unusual case of particular disease (hypothesise about indigestion of contaminated dairy product)	NA

[a] Dohoo et al. (2003), In: Veterinary Epidemiologic Research, AVC Inc., Charlottetown; Chapter 7: Introduction to observational studies, p 142.
[b] Not applicable as descriptive studies cannot evaluate associations.

Table 5: Criteria and scoring system used to assess differences of internal validity between studies identified in the systematic review.

Criteria	Description	Score
Study design	Certain types of observational studies provide better evidence for causality than others	Experiment = 10 Cohort = 8 Case-control (population based) = 6 Case-control (hospital based) = 4 Cross-sectional = 3 Outbreak investigation with denominator = 3
Number of participants	Studies with a larger sample size are likely to provide more representative results	≥ 100 = 5 50 – 99 = 3 < 50 = 1
Confounding	Studies that control for confounding at the design stage (randomisation & matching) provide stronger evidence of causation.	Randomisation = 10 Matching at design stage = 8 Multivariable techniques used = 6 Stratification used = 4 Not addressed = 0
Misclassification of disease status	Studies that have a case definition that includes testing to ensure the agent is present are less likely to have misclassification of the disease status	Case definition given = 10 Test participants positive for causal agent or antibodies = 8 Not addressed = 0
Misclassification of exposure status	Studies that testing suspect product or excluding other exposure are less likely to have misclassification bias	Testing suspect product (milk, cheese or similar) positive for causal agent = 8 Other possible exposure factors excluded = 5 Identification of source of exposure by interview = 3 Patient's history = 1 Not addressed = 0
Response rate	Studies with low a response rate are more likely to be have selection bias present	> 80 = 10 50 – 79 = 4 < 50 = 2 Not reported = 0

2.5 Scoring causality and relevance

Type 1 papers that were thought to have adequate internal validity (i.e. internal validity score ≥ 25) were scored for causality and relevance to New Zealand. When calculating the causality score, each study was reviewed for evidence of causality using three of Hill's criteria for causation (Hill (1965))[10]: (i) temporality, (ii) strength of association, and (iii) evidence of dose response. The method used to score each of these criteria is described in Table 6. In articles where unadjusted relative risk[11] or odds ratios[12] were not reported, the appropriate value (i.e. odds ratio for a case-control study and relative risk for all other studies) was calculated if sufficient data were available. The causality score was calculated by summing the score for each of the three criteria. For any article, the minimum causality score for a paper was three and the maximum was nine, with greater departures from three indicating that the article demonstrates a stronger causal association between raw milk and/or raw milk product and disease/pathogen of concern.

The final part of the systematic review focused on the applicability of evidence to the New Zealand situation – the external validity of a study – by assessing the article relevance to New Zealand. The relevancy score took into consideration two factors: (i) the country where the study was conducted, and (ii) the year of publication. Studies from countries with different production systems to New Zealand and lower health status than New Zealand were considered less relevant to New Zealand, and it was believed that results of recent studies represent the current situation better than older publications. Therefore papers published before 1945 (in respect of World Wars situations) were ranked as 'weak', while studies conducted between the Second World War and the introduced regulations on dairy products in the UK in 1995 were assessed as 'moderate'; it was thought that studies conducted after 1995 do represent the current situation very well. Table 7 describes the semi-quantitative scoring system used to assess relevancy to New Zealand. The relevancy score was then calculated by summing the score for the two criteria. Scores for a paper could range from two to 10, with higher numbers indicating that the paper was of greater relevance to the New Zealand situation.

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[10] Hill A.B., The environment and disease: association or causation? *Proceedings of the Royal Society of Medicine* (1965); 58:295-300.

[11] Relative risk (RR) measures how many times more (or less) probable exposed individuals will become diseased relative to non-exposed individuals.

[12] Odds ratio (OR) measures the odds of disease in exposed individuals compared to odds of disease in non-exposed individuals.

Table 6: Hill's criteria and scoring system used to assess differences of causality between studies identified in the systematic review.

Criteria	Description	Score
Temporality	Consumption of dairy product must precede adverse health effect (Is incubation time realistic?)	Evidence of temporality = 3 Insufficient evidence to determine temporality = 1
Strength of association	The higher a significant relative risk or odds ratio the stronger the indication for an association	Unadjusted relative risk or odds ratio significant and ≥ 3 = 3 Unadjusted relative risk or odds ratio significant and < 3 = 2 Unadjusted relative risk or odds ratio non-significant = 1
Dose response relationship	Number of disease incidence or clinical signs increases with higher dose of consumed pathogens	Evidence of a dose response relationship = 3 Insufficient evidence to determine a dose response relationship = 1

Table 7: Relevancy criteria and scoring system used to rank the applicability to the New Zealand situation (external validity of evidence).

Criteria	Description	Score
Country/region study conducted	Studies from countries non-equivalent to New Zealand were ranked lower	Australia, New Zealand = 5 North America, Western Europe, UK = 3 Eastern Europe, South America, Arabic countries = 1
Year of publication/ incidence	Recent studies represent current situation better than older publications	2008-1996 = 5 1995-1946 = 3 Before and 1945 = 1

2.6 Data synthesis

The evidence of a causal link between the pathogen and consumption of raw milk and/or raw milk products was considered separately for each of the pathogens in Table 1. The first step was to determine, for each pathogen, the number of Type 1 studies with adequate internal validity (i.e. interval validity score ≥ 25). We considered there to be insufficient evidence to objectively evaluate, if there was a causal link between consumption of raw milk and infection with a particular pathogen if less than four Type 1 studies with adequate internal validity were available. Summary measures of causality and relevance were calculated for all agents with greater than or equal to four Type 1 studies with adequate internal validity.

The summary measures for causality were mean and range of causality scores for each Type 1 study with an internal validity score greater than 25. The mean causality for each pathogen was interpreted as follows:

- <5 the evidence provided weak evidence of a causal link;
- 5-6 the evidence provided moderated evidence of a causal link; and
- >6 the evidence provided strong evidence of a causal link.

The range was a measure of the variability in the available data and was interpreted as follows:

- 0 there was no variability in the evidence;
- <3 there was low variability in the evidence;
- 3-5 there was moderate variability in the evidence; and
- 6 there was high variability in the evidence.

Should the variability for a pathogen be classified as either moderate or high, the results needed to be interpreted with caution and reviewed when new information is published.

In order to summarise the relevancy of the information, we calculated the mean relevancy score for the Type 1 studies with adequate internal validity. The mean was interpreted as follows:

- <5 low relevance to New Zealand,
- 5-6 moderate relevance to the New Zealand situation,
- 7-8 high relevance to the New Zealand situation;

- >8 extremely relevant to the New Zealand situation.

No attempt was made to combine the causality and relevance score.

3 Results

3.1 Database percentage accuracy

Primary screening of returns from database searches (retrieved articles) identified a total of 291 papers (potentially relevant articles) with evidence of adverse health effect(s) in humans after consumption of dairy products. After elimination of genuine duplicates and duplicate reports of results (same study or outbreak published more than once), 272 articles were considered as potentially relevant for further examination.

The number of retrieved articles and relevant articles for each article database including percentage accuracy is summarised in Table 8. The lowest percentage accuracy was calculated for Web of Knowledge, although it retrieved the highest number of relevant articles, followed by PubMed, Google Scholar and ScienceDirect. From the number of relevant articles 1.1% (3/272) was identified by all four databases, 13.2% (36/272) by three databases, 44.5% (121/272) by two databases and 83.8% (228/272) by a single database. Eleven articles/reports were retrieved from the Internet searching websites of Public Health Agencies and Food Safety Authorities, whereas 33 articles were found by scanning citations of relevant articles that were not identified by any database.

Table 8: Number of retrieved and relevant articles and the percent (%) accuracy for each database used to search for articles.

Database	Retrieved articles	Relevant articles	% accuracy
Google Scholar	796	60	7.5
PubMed	747	117	15.7
ScienceDirect	151	23	15.2
Web of Knowledge	6,110	188	3.1

3.2 Characteristics of studies included in the preliminary list

A frequency distribution of articles by their year of publication is presented in Figure 2. The majority of relevant articles were published within the last three decades (1981 to the first half of 2008), whereas 22.4% (61/272) were published from 1923 to 1980. Of the 272 articles considered relevant 84 (31%) were classified as Type 1 studies. Further details of these 84 Type 1 studies can be found in Appendix II. The remainder of the studies comprised of Type 2 studies (see summary outcomes and bibliography in Appendices III and IV) and review articles (*n* = 30, % =11). Details of the review articles can be found in Appendix V.

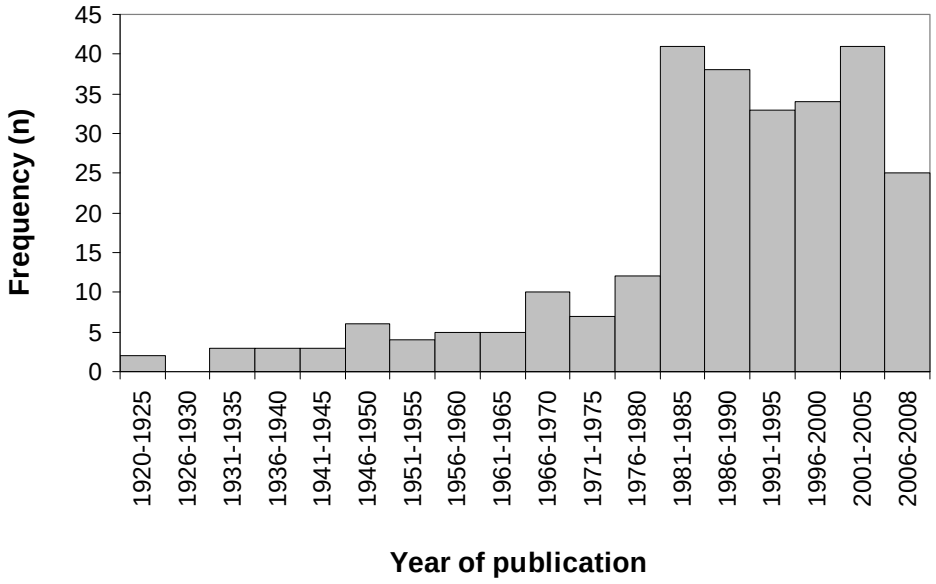

Figure 2: Number of articles retrieved for a systematic review of adverse health effects associated with consumption of raw milk by year of publication (*n* = 272).

3.3 Overview of papers included in the systematic review

Table 9 describes the key features of the Type 1 studies that were included in the systematic review. Almost half of the articles were categorised as population based case-control studies (40/84), the next most common study types were hospital-based case-control studies (16/84) and outbreak investigations with a denominator (12/84). The majority of articles referred to incidences of food poisoning in North America (39/84). In over 50% (44/84) of studies raw milk was reported as the most likely vehicle of infection and unpasteurised cheese was associated with human infection in 23% (19/84) of articles. In 83% (70/84) of studies, dairy product(s) of bovine origin were identified as the source of infection. Twenty seven of the studies were related to bacterial infections caused by *Campylobacter* spp. (27/84) and three articles were not in association with any of the pathogens listed in Table 1 but clearly investigated the influence of raw milk consumption. Therefore, the decision was made to include the three papers in the systematic review. In two other publications the causal agent could not be identified either because the causal agent has as yet not been determined (Brainerd diarrhoea) or the agent was not detected in dairy product or the patient.

Table 9: Number (percentage) of Type 1 studies (n = 84) selected for a systematic review, stratified by country/region where the study was conducted, study design, study size, dairy product, species (origin of dairy product), and type of disease developed.

Category	Level	Number (%) of studies
Country/region	Arabic countries [a]	3 (4)
	Australia	3 (4)
	Eastern Europe [b]	4 (5)
	New Zealand	3 (4)
	North America	39 (46)
	South America [c]	2 (2)
	United Kingdom (UK) [d]	11 (13)
	Western Europe[e] (excl. UK)	19 (23)
Study design	Experiment	4 (5)
	Cohort	7 (8)
	Case-control (population-based)	40 (48)
	Case-control (hospital-based)	16 (19)
	Cross-sectional	5 (6)
	Outbreak investigation with denominator	12 (14)
Study size	≥ 100	40 (48)
	50 – 99	25 (30)
	< 50	19 (23)
Dairy product	Raw milk	44 (52)
	Unpasteurised cheese	19 (23)
	Raw milk and unpasteurised cheese	5 (6)
	Raw milk and unpasteurised cream	2 (2)
	Pasteurised milk or cheese or yoghurt, known to be contaminated	6 (7)
	Pasteurised milk or butter	3 (4)
	Milk-powder	2 (2)
	Milk and soft cheese	2 (2)
	Unknown	1 (1)
Species	Cattle	70 (83)
	Goat	6 (7)
	Cattle and goat	2 (2)
	Sheep	2 (2)
	Sheep and goat	1 (1)
	Cattle, goat, sheep, and camel	1 (1)
	Unknown	2 (2)
Disease	Brucellosis	6 (7)
	Campylobacteriosis	27 (32)
	Q fever (*Coxiella burnetii* infection)	5 (6)
	E.coli infection	7 (8)
	Listeriosis	9 (11)
	Salmonellosis	10 (12)
	Shigellosis	2 (2)
	Staphylococcus infection	5 (6)
	Streptococcus infection	3 (4)
	Tuberculosis (*Mycobacterium bovis* infection)	3 (4)
	Yersiniosis	2 (2)
	Cancer	1 (1)
	Crohn's disease	1 (1)
	Cryptosporidiosis	1 (1)
	Unknown causal agent	2 (2)

[a] Iran, Saudi-Arabia, and Yemen; [b] Greece, Lithuania, and Russia; [c] Brazil; [d] United Kingdom included Scotland, Wales, England, and Northern Ireland; [e] Sweden, France, Finland, Denmark, Czech Republic, Belgium, and Spain.

3.4 Results for specific pathogens

3.4.1 Brucella spp.

Searches identified a total of 37 articles describing an association between brucellosis in humans and the consumption of unpasteurised dairy products. Despite the large number of published papers, we were somewhat limited in our ability to evaluation causation as only six articles were classified as Type 1 (Table 10). Three of the studies were conducted in Arabic countries where *Brucella* is endemic and the consumption of unpasteurised raw milk (and cheese) from goats, sheep, and camel is a traditional practice. There was only one study from Western Europe which reported an outbreak that was most likely caused by unpasteurised cheese made of goat milk. All of the Type 1 studies (n = 6) had acceptable internal validity. The mean causality score and the range in scores were four and two, respectively. Therefore, the evidence provides weak evidence of a causal link. Furthermore, there was low variability in scores, indicating consistency amongst the six studies. Despite the majority of studies having been conducted in Arabic countries, the results have moderate relevance to the New Zealand situation (Mean Relevancy Score = 6).

3.4.2 Campylobacter spp.

Database searching identified 51 articles describing campylobacteriosis in humans following the consumption of unpasteurised milk and/or products made of raw milk. Twenty-seven of these studies were classified as Type 1 studies. Sixteen of the studies were conducted in North America and in all but one study, raw milk of bovine origin was considered as a source of *Campylobacter* infection (Table 11). Four of these papers had an unacceptable internal validity score and were not considered when calculating summary statistics for *Campylobacteria*. A fifth paper by Steele et al. (1978) was also excluded, despite having a perfect score for causality, because it was not clear from the evidence presented in the article, whether the experiment used raw or pasteurised milk. The mean causality score in the remaining 22 was five, and as such the evidence was said to provide moderate support for a causal link between the consumption of unpasteurised milk products and campylobacteriosis in humans. However, there was high variability in the evidence with a range of six for causality scores which suggests careful interpretation of available data. Nonetheless, the relevancy score for these studies was seven, indicating that the results were highly relevant to the New Zealand situation.

3.4.3 E.coli spp.

Literature searches identified 26 published studies investigating the association between *E.coli* infections in humans and the consumption of unpasteurised milk or dairy products made of raw milk. Seven of these studies were classified as Type 1 (Table 12) and 19 as Type 2. All Type 1 studies were published within the past two decades and reported outbreaks in North America, Western Europe and the United Kingdom. The likely sources of infection were raw milk, unpasteurised cheese of bovine and caprine origin as well as other pasteurised dairy products. In three outbreak investigations, the vehicle of infection was thought to be pasteurised milk, cheese curds and yoghurts that became contaminated after pasteurisation as a result of *E.coli* contaminated raw milk or faecal matter (Durch et al. (2000); Moore et al. (1995); Morgan et al. (1993)). Given, there was a possibility that the contamination may not have been due to raw milk we did not consider these papers further. The remaining four studies had acceptable internal validity, scored five for causality and eight for relevancy. Therefore, the evidence provided moderate support for a causal relationship between *E.coli* infection in humans and consumption of unpasteurised milk and dairy products. Furthermore, there was no variability and the results were highly relevant to New Zealand.

3.4.4 Listeria monocytogenes

Literature searches identified nine Type 1 studies (Table 13) and 12 Type 2 studies. The nine Type 1 studies were limited to North America and Western Europe. In six of the articles listeriosis was associated with the consumption of raw milk and unpasteurised cheese of bovine origin, while pasteurised milk and butter were the possible sources of infection in two outbreaks (Fleming et al. (1985); Lyytikainen et al. (2000)). In one outbreak investigation cheese could not be identified as a vehicle of infection with certainty (Riedo et al. (1994)) and as such the study was not considered when summarizing the causality and relevance score. A second Type 1 study was also excluded because the internal validity score was less than 25. In the remaining seven Type 1 studies the mean causality score and relevancy score were five and six, respectively. Therefore, the evidence is of high relevance to New Zealand and provides moderate support for a causal relationship between consumption of raw milk and raw milk products and infection of listeriosis. It is noteworthy that there was moderate variability in the causality scores for each study. One of the reasons for the lower causality is that the prolonged incubation period of listeriosis makes it very difficult to prove temporality when using a case-control study design.

3.4.5 Salmonella serovars

Database searches identified a total of 38 studies investigating the association of salmonellosis in humans and the consumption of raw milk or unpasteurised cheese: ten were Type 1 (Table 14) and 28 Type 2 studies. All but one of the Type 1 studies were conducted in North America or Western Europe. Raw milk and unpasteurised cheese of bovine origin as possible sources of infection were the most common sources of infection. In one outbreak investigation, pasteurised cheese was identified as the vehicle of infection but was most likely contaminated during the manufacture and processing (Hedberg et al. (1992)). Given that disease in Hedberg et al. (1992) cannot definitively be related to raw milk exposure, it was not considered when determining the summary measures for causality and relevancy. In the remaining nine studies, the mean score for causality was five, the range in causality scores was four and the mean relevancy score was eight. Therefore, the strength of evidence supporting a causal link between salmonellosis and consumption of raw milk and unpasteurised cheese is moderate and the results are extremely relevant to New Zealand. There is, however, moderate variability in scores which indicates that the results should be interpreted with caution and subject to review.

3.4.6 Coxiella burnetii

A total of 14 articles were identified when searching for *Coxiella burnetii*, the agent responsible for Q fever, of which only five of these studies were classified as Type 1 studies (Table 15). Of the five Type 1 studies only two had adequate internal validity to be considered further. These two studies provided moderate evidence of a causal relationship between Q fever and consumption of raw milk products. However, two studies are insufficient to draw inferences about causality. In conclusion, due to the lack of good research studies, it is difficult to evaluate any association objectively and as such no conclusions can be drawn.

3.4.7 Mycobacterium bovis

A total of 14 studies describing human health impacts after drinking raw milk or raw milk products contaminated with *Mycobacterium bovis* were identified but only three were classified as Type 1 studies (Table 15). Of these three studies only two studies had adequate internal validity, both with causality score of five and relevancy scores of six and eight. Considering the lack of good research studies, it is difficult to evaluate any association objectively and therefore, no conclusions can be drawn.

3.4.8 Shigella spp.

Only two publications were found to have documented outbreaks of shigellosis in humans and both were classified as Type 1 studies (Table 15). Both outbreaks occurred in Europe and were linked to milk products of bovine origin. In one study unpasteurised cheese was reported as the likely vehicle of infection (Zagrebneviene et al. (2005)), whereas cross-contamination after pasteurisation was the possible source of infection in the other case (Garcia-Fulgueiras et al. (2001)). Considering the lack of good research studies, it is difficult to evaluate any association between raw milk products and infection with *Shigella* spp. objectively, and, therefore no conclusions can be drawn from these two studies.

3.4.9 Staphylococcus spp.

Literature searches identified a total of 13 studies investigating the association between *Staphylococcus* infection in humans and the consumption of raw milk/dairy products made of unpasteurised milk but only five were Type 1 studies (Table 15). Mainly unpasteurised dairy products of bovine origin were identified as the likely source of infection. Cheese, cross-contaminated with *Staphylococcus* pathogens after pasteurisation, was the suspect vehicle of infection in one study (Jelastopulu et al. (2006)), while spray-dried milk powder was thought to be the likely cause of outbreak in another study (Armijo et al. (1957)). Interestingly, all four studies were able to show evidence of temporality and reported strong statistical associations. However, the internal validity in four of the five papers was not acceptable, and as such there was insufficient evidence to assess an association objectively, if there is a causal link between exposure to raw milk and/or dairy products made from raw milk and infection with *Staphylococcus*.

3.4.10 Streptococcus spp.

There were 13 publications found to have studied the occurrence of *Streptococcus* infection in humans in association with the consumption of raw milk or unpasteurised cheese contaminated with *Streptococcus* pathogens but only three were Type 1 studies (Table 15). All three studies identified dairy products of bovine origin as vehicle of infection. Inadequately pasteurised cheese was believed to be the cause of outbreak in one study (Bordes-Benitez et al. (2006)), while the other two were linked to raw milk and unpasteurised cheese processing raw milk from cows with *Streptococcus* mastitis. Due to the lack of research, there is not sufficient evidence to support the hypothesis that consumption of raw

milk/unpasteurised cheese was the causal factor of disease. This conclusion will need to be reviewed if additional information becomes available.

3.4.11 Yersinia spp.

Only two publications were found investigating the association between yersiniosis in humans and the consumption of dairy products contaminated with *Yersinia* spp. (Table 15). The American study was an outbreak investigation where pasteurised milk became contaminated with *Yersinia* pathogens probably at the dairy. In contrast, the New Zealand study focused on the identification of risk factors for yersiniosis including raw milk as a possible source of infection. Only the American study could show some evidence for temporality and strong statistical association between the consumption of *Yersinia* contaminated milk and the disease in humans. In the New Zealand study, no statistical association was identified with drinking raw milk and the incidence of yersiniosis. Based on the very small number of studies, there is not sufficient evidence to support a causal association between consumption of raw milk and yersiniosis in humans.

3.4.12 Other pathogens/diseases

Database searches identified another five studies investigating the association between consumption of raw milk/unpasteurised cheese and human diseases not listed in Table 1 (Table 15). In two of the studies, the causal pathogen could not be identified as it was unknown (Brainerd diarrhoea in Osterholm et al. (1986)) or could not be detected during the investigation (neither in the dairy product nor the patient) (Maguire et al. (1991)). The cancer study (Sellers et al. (2008)) did not specify the species when enquiring about past exposure of drinking raw milk and the study by Van Kruiningen et al. (2005) aimed to identify risk factors for Crohn's disease of which the causal pathogen is still unknown. Only the Australian study by Harper et al. (2002) was able to find the causal agent (*Cryptosporidium*) within this group of 'miscellaneous' pathogens/diseases. Although all four studies (except cancer study) have found statistical associations between the consumption of raw milk or unpasteurised cheese and disease in humans, no study could provide evidence for temporality and therefore it is very questionable, whether there is a causal relationship between consumption of raw milk and/or raw milk products and any of these diseases.

3.5 Conclusions

Table 16 summarises the results for each of the pathogens. The evidence provided moderate support for a causal link between the consumption raw milk/raw milk products and infection with the following pathogens:

- *Campylobacter* spp.;
- *E. coli* spp.;
- *Listeria monocytogenes*; and
- *Salmonella* serovars.

The evidence also provided, albeit weak, support for a causal link between infection with *Brucella* and the consumption of raw milk products. Owing to the shortage of studies and/or shortage of studies with adequate internal validity, it was not possible to objectively evaluate if there was a causal link between exposure to raw milk and products made from raw milk and the following pathogens/diseases:

- *Coxiella burnetii*;
- *Mycobacterium bovis*;
- *Shigella*;
- *Staphylococcus*;
- *Streptococcus*;
- *Yersinia*;
- Cancer;
- Crohn's disease; and
- *Cryptosporidium*.

Toxoplasma infections in humans linked to consumption of raw milk/raw milk products were only reported in Type 2 studies and therefore insufficient to prove any causal association; no literature was found for *Bacillus cereus* reporting human disease in association with the consumption of raw milk and/or raw milk products.

A meta-analysis was not conducted as part of this review; however, the available literature was evaluated to determine whether there was sufficient information to be included in a meta-analysis. Based on our findings of evidence included in this systematic review, there was neither adequate qualitative agreement between studies described, nor sufficient quantitative data to warranty a meta-analysis.

Table 10: Systematic review scores for causality and relevancy of articles documenting adverse health effects in humans after consumption of raw milk/dairy products made of raw milk contaminated with *Brucella* spp. Results presented ordered by causality score.

Internal validity acceptable?[a]	Reference	Year	Country	Product	Species	Causality score	Relevancy score
Yes	Jordan	1931	North America	Raw milk, unpasteurised cream	Cow	3	4
Yes	Almuneef	2004	Arabic country	Raw milk	Cow, goat, sheep, camel	4	6
Yes	Hadjichristodoulou	1999	Eastern Europe	Raw milk, unpasteurised cheese	Unknown	4	6
Yes	Al-Shamahy	2000	Arabic country	Raw milk	Sheep, goat	5	6
Yes	Martínez	2003	Western Europe	Unpasteurised cheese	Goat	5	8
Yes	Sofian	2008	Arabic country	Raw milk, unpasteurised cheese	Sheep	5	6

[a] Yes indicates that the article had an internal validity score ≥ 25.
No indicated that the article had an internal validity score <25.

Table 11: Systematic review scores for causality and relevancy of articles documenting adverse health effects in humans after consumption of raw milk/dairy products made of raw milk contaminated with *Campylobacter* spp. Results presented ordered by causality score.

Internal validity acceptable?[a]	Reference	Year	Country	Product	Species	Causality score	Relevancy score
No	Blaser	1979	North America	Raw milk	Cow	-	-
No	Taylor	1979	North America	Raw milk	Cow	-	-
No	Brieseman	1984	New Zealand	Raw milk	Cow	-	-
No	Peterson	2003	North America	Raw milk	Cow	-	-
Yes	Church Potter	2003	North America	Raw milk	Cow	3	8
Yes	Neimann	2003	Western Europe	Raw milk	Cow	3	8
Yes	Harris	1987	North America	Raw milk	Goat	3	6
Yes	Tenkate	2001	Australia	Milk, soft cheese	Cow	3	10
Yes	Eberhart-Phillips	1997	New Zealand	Raw milk, unpasteurised cream	Cow	4	10
Yes	Wright	1983	UK	Raw milk	Cow	5	6
Yes	Black	1988	North America	Milk-powder	Cow	5	6
Yes	Michaud	2004	North America	Raw milk	Cow	5	8
Yes	Morgan	1994	UK	Raw milk	Cow	5	6
Yes	Carrique-Mas	2005	Western Europe	Raw milk	Cow	5	8
Yes	Friedman	2004	North America	Raw milk	Cow	5	8
Yes	Harris	1986	North America	Raw milk	Cow	5	6
Yes	Fahey	1995	UK	Raw milk	Cow	5	6
Yes	Hopkins	1984	North America	Raw milk	Cow	5	6

Internal validity acceptable?[a]	Reference	Year	Country	Product	Species	Causality score	Relevancy score
Yes	Studahl	2000	Western Europe	Raw milk	Cow	5	8
Yes	Schmid	1987	North America	Raw milk	Cow	5	6
Yes	Potter	1983	North America	Raw milk	Cow	7	6
Yes	Taylor	1982	North America	Raw milk	Cow	7	6
Yes	Klein	1986	North America	Raw milk	Cow	7	6
Yes	Kornblatt	1985	North America	Raw milk	Cow	7	6
Yes	Birkhead	1988	North America	Raw milk	Cow	7	6
Yes	Evans	1996	UK	Raw milk	Cow	7	8
Yes	Steele	1978	Australia	Milk[b]	Cow	9	8

[a] Yes indicates that the article had an internal validity score ≥ 25.
No indicates that the article had an internal validity score <25.
[b] Insufficient evidence in the article to determine if the milk was pasteurised or unpasteurised and as such this source was not considered when determining the overall causality and relevancy scores.

Table 12: Systematic review scores for causality and relevancy of articles documenting adverse health effects in humans after consumption of raw milk/dairy products made of raw milk contaminated with *E.coli* spp. Results presented ordered by causality scores.

Internal validity acceptable?[a]	Reference	Year	Country	Product	Species	Causality score	Relevancy score
Yes	Moore	1995	North America	Pasteurised milk[b]	Cow	3	6
Yes	Bhat	2007	North America	Raw milk	Cow	5	8
Yes	Bielaszewska	1997	Western Europe	Raw milk	Goat	5	8
Yes	Deschênes	1996	Western Europe	Unpasteurised cheese	Cow, goat	5	8
Yes	Durch	2000	North America	Cheese curds[b]	Cow	5	8
Yes	Jensen	2006	Western Europe	Raw milk	Cow	5	8
Yes	Morgan	1993	UK	Yoghurt[b]	Cow	5	6

[a] Yes indicates that the article had an internal validity score ≥ 25.
No indicates that the article had an internal validity score <25.
[b] Product was thought to be contaminated after pasteurisation with raw milk but the evidence was not conclusive and as such this source was not considered when determining the overall causality and relevancy scores.

Table 13: Systematic review scores for causality and relevancy of articles documenting adverse health effects in humans after consumption of raw milk/dairy products made of raw milk contaminated with *Listeria monocytogenes* pathogens. Results presented ordered by causality score.

Internal validity acceptable?[a]	Reference	Year	Country	Product	Species	Causality score	Relevancy score
No	Goulet	1995	Western Europe	Unpast. cheese	Cow	-	-
Yes	Lyytikainen	2000	Western Europe	Pasteurised butter[b]	Cow	3	8
Yes	Jensen	1994	Western Europe	Raw milk	Cow	3	6
Yes	Schuchat	1992	North America	Unpast. cheese	Cow	4	6
Yes	Fleming	1985	North America	Pasteurised milk	Cow	5	6
Yes	Linnan	1988	North America	Unpasteurised cheese	Cow	5	6
Yes	MacDonald	2005	North America	Unpasteurised cheese	Cow	5	8
Yes	Carrique-Mas	2003	Western Europe	Raw milk	Cow, goat	6	8
Yes	Riedo	1994	North America	Cheese?[c]	Cow	7	6

[a] Yes indicates that the article had an internal validity score ≥ 25.
No indicates that the article had an internal validity score <25.
[b] Product was thought to be contaminated after pasteurisation with raw milk but the evidence was not conclusive and as such this source was not considered when determining the overall causality and relevancy scores.
[c] Cheese was not confirmed as the vehicle of infection and as such this source was not considered when determining the overall causality and relevancy scores.

Table 14: Systematic review scores for causality and relevancy of articles documenting adverse health effects in humans after consumption of raw milk/dairy products made of raw milk contaminated with *Salmonella* serovars. Results presented ordered by causality score.

Internal validity acceptable?[a]	Reference	Year	Country	Product	Species	Causality score	Relevancy score
Yes	Austin	2008	North America	Unpasteurised cheese	Cow	3	8
Yes	CDC[b]	1984	North America	Raw milk	Cow	5	6
Yes	Cody	1999	North America	Unpasteurised cheese	Cow	5	8
Yes	De Valk	2000	Western Europe	Unpasteurised cheese	Cow	5	8
Yes	Desenclos	1996	Western Europe	Unpasteurised cheese	Goat	5	8
Yes	Haeghebaert	2003	Western Europe	Unpasteurised cheese	Cow	5	8
Yes	Hedberg	1992	North America	Pasteurised cheese[b]	Cow	5	6
Yes	Mazurek	2004	North America	Raw milk	Cow	5	8
Yes	Villar	1999	North America	Unpasteurised cheese	Cow	5	8
Yes	Maguire	1992	UK	Unpasteurised cheese	Cow	7	6

[a] Yes indicates that the article had an internal validity score ≥ 25.
No indicates that the article had an internal validity score <25.
[b] Product was thought to be contaminated after pasteurisation with raw milk but the evidence was not conclusive and as such this source was not considered when determining the overall causality and relevancy scores.

Table 15: Systematic review scores for causality and relevancy of articles documenting adverse health effects in humans after consumption of raw milk/dairy products made of raw milk contaminated, ordered by pathogen/disease.

Agent/Disease	Internal validity acceptable?[a]	Reference	Year	Country	Product	Species	Causality score	Relevancy score
Cancer	Yes	Sellers	2008	North America	Raw milk	?	3	8
Coxiella burnetii	No	Brown	1968	United Kingdom	Raw milk	Cow	-	-
	No	Fishbein	1992	Western Europe	Raw milk Unpasteurised cheese	Goat	-	-
	No	Brouqui	1993	Western Europe	Raw milk	Cow	-	-
	Yes	Jorm	1990	United Kingdom	Raw milk	Goat	5	6
	Yes	Krumbiegel	1970	North America	Raw milk	Cow	5	6
Crohn's disease	Yes	Van Kruiningen	2005	Western Europe	Raw milk Unpasteurised cheese	Cow	5	8
Cryptosporidium	Yes	Harper	2002	Australia	Raw milk	Cow	5	10
Mycobacterium bovis	No	Black	1961	United Kingdom	Raw milk	Cow	-	-
	Yes	Besser	2001	North America	Raw milk Unpasteurised cheese	Cow	5	8
	Yes	Coker	2006	Eastern Europe	Raw milk	Cow	5	6
Shigella	Yes	Garcia-Fulgueiras	2001	Western Europe	Pasteurised cheese[b]	Cow	4	8
	Yes	Zagrebneviene	2005	Eastern Europe	Unpasteurised cheese	Cow	5	6

Agent/Disease	Internal validity acceptable?[a]	Reference	Year	Country	Product	Species	Causality score	Relevancy score
Staphylococcus	No	Bone	1989	United Kingdom	Unpasteurised cheese	Sheep	-	-
	No	Cerqueira	1994	South America	Unpasteurised cheese	Cow	-	-
	No	Crabtree	1934	North America	Raw milk	Cow	-	-
	No	Armijo	1957	North America	Milk-powder	Cow	-	-
	Yes	Jelastopulu	2006	Eastern Europe	Cheese	Cow	7	6
Streptococcus	No	Dublin	1943	North America	Raw milk	Cow	-	-
	Yes	Balter	2000	South America	Unpasteurised cheese	Cow	4	6
	Yes	Bordes-Benitez	2006	Western Europe	Unpasteurised cheese	Cow	5	8
Unknown	No	Maguire	1991	United Kingdom	Unpasteurised cheese	Cow	-	-
	Yes	Osterholm	1986	North America	Raw milk	Cow	5	6
Yersinia	Yes	Satterthwaite	1999	New Zealand	Raw milk	Cow	3	10
	Yes	Black	1978	North America	Pasteurised milk	Cow	7	6

[a] Yes indicates that the article had an internal validity score ≥ 25.
No indicates that the article had an internal validity score <25.
[b] Product was thought to be contaminated after pasteurisation with raw milk but the evidence was not conclusive and as such this source was not considered when determining the overall causality and relevancy scores.

Table 16: Total number of studies, the number of Type 2[a] studies, Type 1[b] studies with adequate internal validity (IV) and Type 1 studies with inadequate IV and mean causality score, range in causality scores and mean relevancy score for each pathogen.

	Number of studies				Causality Score		
Pathogen	**Type 2**	**Type 1- Inadequate IV[c]**	**Type 1- adequate IV[d]**	**Total**	**Mean**	**Range**	**Mean Relevancy Score**
Brucella spp.	31	0	6	37	Low	Low	Moderate
Campylobacter spp.	24	4	23	51	Moderate	High	High
E.coli spp.	19	0	7	26	Moderate	None	High
Listeria monocytogenes	12	1	8	21	Moderate	Moderate	High
Salmonella spp.	28	0	10	38	Moderate	Moderate	High
Coxiella burnetii	9	3	2	14	Insufficient	Insufficient	Insufficient
Mycobacterium bovis	11	1	2	14	Insufficient	Insufficient	Insufficient
Shigella spp.	0	0	2	2	Insufficient	Insufficient	Insufficient
Staphylococcus spp.	8	4	1	13	Insufficient	Insufficient	Insufficient
Streptococcus spp.	10	1	2	13	Insufficient	Insufficient	Insufficient
Yersinia spp.	0	0	2	2	Insufficient	Insufficient	Insufficient
Toxoplasma	3	0	0	3	Insufficient	Insufficient	Insufficient

[a] 'Type 2' studies are comprised of outbreak investigations (without a denominator), surveys, case reports, and case series.
[b] 'Type 1' studies are randomised control trials, cohort, case-control, cross-sectional studies, and outbreak investigations with information about the number of exposed individuals.
[c] 'Type 1' studies with and internal validity scores <25.
[d] 'Type 1' studies with and internal validity scores ≥ 25.

4 Discussion of methodology

The overriding concern, when undertaking this systematic review, was the general lack of studies and the lack of studies with good internal validity. We do not believe that this was because we missed relevant articles in our searching, as we searched widely and used keywords to maximise the retrieval of relevant articles for each selected pathogen. In fact, the use of keywords to maximise retrieval resulted in a large number of irrelevant articles being selected, as indicated by the low database percentage accuracy. One of the reasons for this was that the keywords used to search databases resulted in the retrieval of a number of articles related to food technology. Considering the topic under review is directly associated with human health and food, it was not possible to design more specific search terms without increasing the likelihood of missing relevant articles.

Caution is advised when using the database accuracy to guide decisions about use of search engines when trying to retrieve relevant literature on a specific topic. For example, Web of Knowledge had the lowest percentage accuracy but produced the highest number of relevant articles. Moreover, the majority of the articles identified in the Web of Knowledge searches were not retrieved by any other database. Therefore, in order to achieve completeness of literature search, it is important to search multiple databases because only a small number of articles appeared in more than one database. Furthermore, it is essential to screen the reference list of all the articles for other relevant articles; this is especially useful when trying to identify studies published before 1950.

Keywords used in search terms have identified articles reporting evidence of human disease associated with the consumption of raw milk and/or dairy products made of raw milk. However, these keywords have also retrieved evidence of pasteurisation failures and contaminations with raw milk after pasteurisations which are basically equivalent to consumers' exposure to unpasteurised milk or unpasteurised dairy products (see Tables 10 to 15 in Results section). In addition, searching websites of food safety authorities and public health and food agencies of several countries (UK, USA, Canada, Ireland, Australia, the European Union) has assured that reports of pasteurisation failures have been included in this systematic review.

A total of 272 primary research articles were identified by the search criteria, but only 84 were classified as Type 1 studies and considered further in the review. The classification system was designed to divide studies into those that by their design could and could not

provide evidence of causation. Specifically, outbreak investigations without information about the total number of people exposed (i.e. denominator data) do not provide any information about those people that did not become ill and as such measures of frequency and association cannot be calculated. One of the reasons why denominator data may not be collected is that during an outbreak the aim of the investigation is to identify the source of infection as quickly as possible to avoid further cases, rather than to collect data that can be used to assess causality. Be that as it may, outbreak investigations without denominator data and cases series do suggest that there may be an association between consumption of raw milk and raw milk products and adverse health effects.

In the current review, the majority of Type 1 studies were outbreak investigations and reports and therefore not of high internal validity; which was reflected in the moderate to low scores for internal validity of the assessed studies and consequently affected the evidence to prove a possible causal relationship. A number of studies were not assessed for causality and relevance as scoring less than 25 for internal validity. These studies were excluded because the results were more likely to be biased, and as such it would not be possible to determine whether the observed effects were true or occurred as a result of bias.

The evidence scored for causality did not provide strong support for a causal relationship between consumption of raw milk and infection with any of the pathogens/agents we considered. This was in part due to the design of the reported studies; only 11/84 articles were identified as experiments or cohort studies implying that the remaining majority of articles (including case-control, cross-sectional, outbreak investigations with given denominator) were limited by their study design to prove a causal relationship; i.e. the design of case-control studies makes it difficult, if not impractical to demonstrate temporality. It was also difficult to prove causality when studying disease with long incubation periods (i.e. Tuberculosis and listeriosis) because infected humans are exposed to a range of other possible risk factors during the incubation period. Thus, it is unfeasible to determine the genuine source of infection. Another reason for low causality scores is that the studies need to report the successful detection of the causal pathogen. However, several outbreak investigations were unable to detect the causal agent, because of various reasons: (i) the food item was already eaten or not available (especially in diseases with long incubation periods); (ii) pathogen was self-destroying over time (cheeses); (iii) diagnostic method to detect pathogenic enterotoxins of toxin-producing pathogens was not developed (e.g. *Staphylococcus* enterotoxin); (iv) irregular excretion of pathogens in species of origin (e.g. *Streptococcus* abscess in udder, *Campylobacter* enteritis); (v) irregular faecal contamination of raw milk. As

a logic consequence, causality could not be demonstrated as the causal agent was not detected in the raw milk product.

The majority of food poisoning incidences (or risk factor studies) were reported from North America, followed by Western Europe and the United Kingdom (UK). This observation was not surprising because public health and food safety aspects are of high importance in these countries. Therefore outbreaks of food poisoning are more likely to be detected and made official in reports and eventually being published in peer reviewed journals. In more than half of the studies, raw milk (of any species) was considered as the most likely vehicle of infection, whereas less than a quarter of articles had inferred unpasteurised cheese as the cause of disease. The difference between raw milk and unpasteurised cheese may be due to differences in the level of exposure that is, more people consume raw milk than unpasteurised cheese. In terms of species, dairy products of bovine origin were identified as the source of infection in 83% (70/84) of studies, which is also likely to reflect consume habits rather than increased risk in bovine dairy products.

Overall, there was no strong evidence for causal relationship, however moderate causal links were found for *Campylobacter* spp., *E. coli* spp., *Listeria monocytogenes*, and *Salmonella* serovars. These pathogens are more or less common in New Zealand, hosting predominantly in animals and are a potential source of infection for humans, in particular via faecal contamination of raw milk. Therefore, we suggest taking these pathogens into considerations when developing 'Standards' for domestic raw milk products, although present literature does not provide strong evidence for a causal relationship.

No attempt was made to combine the causality and relevance score because policy makers would need to consider the evidence differently, depending on whether one was assessing the risk for a domestic or imported dairy product(s). Specifically, when considering dairy products made from New Zealand raw milk, it would be necessary to consider (i) if the pathogen is present in New Zealand and whether (ii) the literature supports a causal link between consumption of raw milk and infection with the pathogen and (iii) if the literature was relevant to the New Zealand situation. In contrast, when considering an imported product, it would be necessary to consider (i) what pathogens are present in the exporting country and then (ii) determine if the literature supports evidence of a causal link between consumption of raw milk and infection with the pathogens of interest. Decision makers may also want to come up with a relevancy scoring system for the exporting country.

5 Discussion of evidence

The systematic review was hampered by a lack of studies and/or studies conducted in a manner that could be used to demonstrate causality. It was not possible to determine whether there is a causal link between consumption of raw milk and infection with *Shigella, Yersinia;* and *Toxoplasma* because we retrieved less than four studies, for each pathogen. The lack of studies could reflect a lack of research. Alternatively, the lack of studies could be because consumption of raw milk and raw milk products rarely results in infections with *Shigella*, *Yersinia* and *Toxoplasma*.

We retrieved in excess of four articles for *Coxiella burnetii* (*n* = 14), *Mycoplasma bovis*, (*n* = 14), *Staphylococcus* spp. (*n* = 13) and *Streptococcus* spp. (*n* = 13). However, for each pathogen, there were less than four Type 1 studies with internal validity scores of ≥ 25 and as such it was not possible to demonstrate a link between consumption of raw milk/raw milk products and infection with *Coxiella burnetii, Mycoplasma bovis, Staphylococcus* spp. and *Streptococcus* spp.

For *Brucella* spp., *Campylobacter* spp., *E.coli* spp., *Listeria monocytogenes*, and *Salmonella* serovars we were able to find low to moderate evidence to support a causal link between consumption of raw milk products and adverse health effects. When this is taken in combination with the relatively high number of Type 2 studies for each pathogen (Table 16), there is a reasonable body of evidence to support the hypothesis, that consumption of raw milk puts an individual at greater risk of being infected with *Brucella* spp., *Campylobacter* spp., *E.coli* spp., *Listeria monocytogenes*, and *Salmonella* serovars.

6 Conclusions

The overriding concern, when undertaking this systematic review, was the overall lack of studies and the lack of studies with good internal validity. The evidence provided moderate support for a causal link between infections associated with *Campylobacter* spp., *E. coli* spp., *Listeria monocytogenes*, *Salmonella* serovars and the consumption of raw milk products; and a weak support of a causal link between consumption of raw milk products and infection with *Brucella* spp. Due to the lack of well designed studies a meta-analysis using the available evidence cannot be conducted.

Appendices

Appendix I: Assessment worksheet

Qu 1: Is the study a 'Type 2' study?

(This includes case-series, case reports, surveys, outbreak investigations without denominator given; for definitions see section 2.6, Table 3)

Yes end assessment here.

No it is a 'Type 1' study, which includes RCT, cohort, case-control, cross-sectional studies, and outbreak investigations with given denominator (for definitions see Section 2.4, Table 4). Therefore assess its internal validity, causality and relevancy using the scoring systems below.

Qu 2: Is this study internally valid?

Criteria	Level	Score	Tick
Study design	Randomised controlled trial (RCT) or experiment.	10	
	Cohort.	8	
	Population based case-control.	6	
	Hospital based case-control.	4	
	Cross-sectional or Outbreak investigation (denominator given).	3	
Number of participants	≥ 100	5	
	50 – 99	3	
	< 50	1	
How was confounding addressed?	Randomisation.	10	
	Matching (sex, age) at the design stage.	8	
	Multivariable techniques used.	6	
	Stratification used.	4	
	It was not adjusted for.	0	
How was misclassification of disease status avoided?	Case definition given (incl. clinical signs).	10	
	Testing participants positive for causal agent (RCT, cohort, case-control, outbreak investigation) or antibodies (cross-sectional).	8	
	It was not addressed / agent not detected.	0	
How was misclassification of exposure status avoided?	Testing suspect product (milk, cheese or similar) positive for causal agent.	8	
	Other possible exposure factors excluded (animal contact, person-to-person contact, environment) or no evidence or negative test results.	5	
	Identification of source of exposure by interview/questionnaire (attack rate).	3	
	Patient's history.	1	
	It was not addressed.	0	
How was the response rate?	> 80	10	
	50 - 79	4	
	< 50	2	
	It was not reported.	0	

Qu 3: Was there any evidence for causality?

Criteria	Level	Score	Tick
Was there any evidence for causality? (Hill's criteria)	*Temporality*		
	Consumption of dairy product preceded adverse health effect (realistic incubation time?)	3	
	No temporality	1	
	Strength of association		
	Unadjusted OR or RR ≥ 3 (strong) and significant	3	
	Unadjusted OR or RR < 3 and significant	2	
	Unadjusted OR or RR non-significant	1	
	Dose-response relationship		
	Evidence of dose-response relationship	3	
	No dose-response relationship	1	

Qu 4: Is this study applicable to the New Zealand situation? (Relevancy ranking)

Criteria	Level	Score	Tick
Country	Australia, New Zealand	5	
	North America, Western Europe, UK	3	
	Eastern Europe, Arabic countries, South America	1	
Year of incidence/ publication	2008-1996	5	
	1995-1945	3	
	Before 1945	1	

Appendix II: Bibliography of Type 1 studies

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Appendix III: Summary of all Type 2 studies

Table A.I: Summary of all Type 2 studies, stratified by agent.

Pathogen	Reference	Year	Country	Product	Species
Brucella	Al Dahouk	2005	Western Europe	Raw milk, unpast. cheese	Goat, sheep
	Al-Eissa	1990	Arabic country	Raw milk	Cow
	Al-Rawi	1989	Arabic country	Butter, cream, unpast. cheese	Cow
	Bingöl	2006	Eastern Europe	Raw milk	Cow
	Bothwell	1960	UK	Raw milk	Cow
	Bothwell	1962	UK	Raw milk	Cow
	Celebi	2007	Eastern Europe	Unpast. cheese	Goat
	Cruickshank	1942	UK	Raw milk	Cow
	Eckman	1975	North America	Unpast. cheese	Cow
	Elkington	1940	UK	Raw milk	Cow
	Galbraith	1969	UK	Unpast. cheese	Sheep
	Galbraith	1984	UK	Raw milk	Cow
	Gomez-Reino	1986	Western Europe	Raw milk, unpast. cheese	Cow
	Henderson	1967	UK	Raw milk	Cow
	Hendricks	1995	Africa	Raw milk	Cow
	Jennings	2007	Arabic country	Raw milk	Unknown
	Lulu	1988	Arabic country	Raw milk, unpast. cheese	Cow, sheep, goat, camel
	Memish	2001	Arabic country	Raw milk, unpast. cheese	Goat, camel
	Mousa	1986	Arabic country	Raw milk	Unknown
	Mousa	1988	Arabic country	Raw milk	Cow, goat, camel
	Public Health Agency	1995	UK	Unpast. cheese	Sheep, goat
	Ramos	2008	Western Europe	Raw milk	Goat
	Sabbaghian	1974	Arabic country	Raw milk	Cow, sheep, goat
	Sharda	1986	Arabic country	Raw milk, unpast. cheese	Cow, sheep, goat, camel
	Steele	1948	North America	Raw milk	Cow
	Street	1975	North America	Unpast. cheese	Goat
	Vogt	1999	Western Europe	Unpast. cheese	Goat
	Wallach	1994	South America	Unpast. cheese	Goat
	Wynne	1985	UK	Unpast. cheese	Cow, goat
	Young	1975	Central America	Unpast. cheese	Goat
	Zaks	1995	Arabic country	Raw milk, unpast. cheese	Goat
Campylo-bacter	Anonymous	1984	North America	Raw milk	Cow
	Atanassova	2001	Western Europe	Raw milk	Cow
	Blaser	1987	North America	Raw milk	Cow
	Finch	1985	North America	Raw milk	Cow
	Harrington	2002	North America	Raw milk	Cow
	Hudson	1984	North America	Raw milk	Cow
	Hutchinson	1985	UK	Raw milk	Cow
	Hutchinson	1985	UK	Raw milk	Goat
	Jones	1981	UK	Raw milk	Cow
	Kálmán	2000	Eastern Europe	Raw milk	Cow
	Korlath	1985	North America	Raw milk	Cow
	Lehner	2000	Western Europe	Raw milk	Cow
	McNaughton	1982	UK	Raw milk	Cow

Table A.I. continued

Pathogen	Reference	Year	Country	Product	Species
Campylo-bacter	Morgan	1985	UK	Raw milk	Cow
	Orr	1995	UK	Raw milk	Cow
	Porter	1980	UK	Raw milk	Cow
	Robinson	1979	UK	Raw milk	Cow
	Robinson	1981	UK	Pasteurised milk	Cow
	Schildt	2005	Western Europe	Raw milk	Cow
	Tettmar	1981	UK	Raw milk	Cow
	Wallace	1980	UK	Raw milk	Cow
	Warner	1986	North America	Raw milk	Cow
	Wood	1992	North America	Raw milk	Cow
	Anonymous	1991	UK	Raw milk	Cow
Coxiella burnetti	Chaillon	2008	Western Europe	Raw milk	Goat
	Connolly	1968	UK	Raw milk	Cow
	Cracea	1989	Eastern Europe	Raw milk	Cow
	Ellis	1983	UK	Raw milk	Cow
	Marmion	1958	UK	Raw milk	Cow
	Poole	1969	UK	Raw milk	Cow
	Public Health Agency of Canada	2000	North America	Pasteurised cheese	Goat
	Tissot Dupont	1992	Western Europe	Raw milk, unpast. cheese	Cow, goat
	Tylewska-Wierzbanowska	1991	Eastern Europe	Raw milk	Cow
E.coli	Allerberger	2001	Western Europe	Raw milk	Cow, goat
	Allerberger	2003	Western Europe	Raw milk	Cow
	Chapman	1993	UK	Raw milk	Cow
	Curnow	1999	UK	Unpast. cheese	Goat
	Espié	2006	Western Europe	Unpast. cheese	Goat
	Honish	2005	North America	Unpast. cheese	Cow
	Jayarao	2006	North America	Raw milk	Cow
	Keene	1997	North America	Raw milk	Cow
	Liptakova	2004	Eastern Europe	Raw milk, cream	Cow
	MacDonald	1985	North America	Cheese	Cow
	Marier	1973	North America	Cheese	Cow
	Martin	1986	North America	Raw milk	Cow
	Møller-Nielsen	2005	Western Europe	Raw milk?	Cow
	O'Brien	2000	UK	Raw milk	Cow
	Public Health Agency	2000	UK	Raw milk	Cow
	Public Health Agency of Canada	2002	North America	Raw milk	Goat
	Public Health Laboratory Service	1976	UK	Raw milk	Cow
	Public Health Laboratory Service	1998	UK	Unpast. cream	Cow
	Schneider	2008	North America	Raw milk	Cow

Table A.I. continued

Pathogen	Reference	Year	Country	Product	Species
Listeria monocytogenes	Azadian	1989	UK	Cheese	Goat
	Bannister	1987	UK	Pasteurised cheese	Cow
	Beninger	1988	North America	Raw milk	Cow
	Büla	1995	Western Europe	Cheese	Cow
	Dalton	1997	North America	Pasteurised milk	Cow
	Doorduyn	2006	Western Europe	Not defined	
	Farber	1990	North America	Unpast. cheese	Cow
	Gilot	1997	Western Europe	Cheese	Cow
	Makino	2005	Asian country	Cheese	Cow
	Oh	1992	Asian country	Raw milk	Unknown
	Public Health Agency of Canada	2003	North America	Unpast. cheese	Cow
	Vogt	1990	North America	Raw milk	Cow
Mycobacterium bovis	Ahmed	1998	India	Raw milk	Cow
	Bohme	2007	Western Europe	Raw milk	Cow
	Brown	1947	UK	Raw milk	Cow
	Dankner	2000	North America	Unpast. cheese	Cow
	Griffith	1944	UK	Raw milk	Cow
	Keidan	1952	UK	Raw milk	Cow
	Oloya	2007	Africa	Raw milk	Cow
	Pande	1995	India	Raw milk	Cow
	Tobiesen	1935	Western Europe	Raw milk	Cow
	Winters	2005	North America	Unpast. cheese	Cow
	Zwanenberg	1956	UK	Raw milk	Cow
Salmonella	Anonymous	1938	UK	Raw milk	Cow
	Anonymous	1973	UK	Raw milk	Cow
	Centers for Disease Control and Prevention	1984	North America	Raw milk	Cow
	Centers for Disease Control and Prevention	2007	North America	Raw milk, unpast. cheese	Cow
	Communicable Disease Surveillance Centre	1985	UK	Raw milk, cream	Cow
	D'Aoust	1985	North America	Unpast. cheese	Cow
	Ellis	1998	North America	Unpast. cheese	Cow
	Fierer	1983	North America	Raw milk	Cow
	Fontaine	1980	North America	Unpast. cheese	Cow
	Hutchinson	1964	UK	Raw milk	Cow
	Kinloch	1923	UK	Raw milk	Cow
	Knox	1963	UK	Raw milk	Cow
	Lennox	1954	UK	Raw milk	Cow
	Lind	2007	North America	Raw milk, unpast. cheese	Cow
	Mateus	2008	UK	Raw milk?	Cow
	McCall	1953	UK	Raw milk	Cow
	Parry	1962	UK	Raw milk	Cow

Table A.I. continued

Pathogen	Reference	Year	Country	Product	Species
Salmonella	Price	1967	North America	Unpasteurised cheese	Cow
	Public Health Laboratory Service	1998	UK	Raw milk	Cow
	Reilly	1983	UK	Raw milk	Cow
	Sharp	1980	UK	Raw milk	Cow
	Small	1979	UK	Raw milk	Cow
	Tacket	1985	North America	Raw milk	Cow
	Talbot	1967	UK	Raw milk	Cow
	Tucker	1946	North America	Unpasteurised cheese	Cow
	Vogt	1981	North America	Raw milk	Cow
	Werner	1979	North America	Raw milk	Cow
	Public Health Laboratory Service	1984	UK	Raw milk	Cow
Staphylococcus	Asao	2003	Asian country	Pasteurised milk, milk-powder	Cow
	de Buyser	1985	Western Europe	Unpasteurised cheese	Sheep
	Gross	1988	Arabic country	Raw milk	Goat
	Ikeda	2005	Asian country	Milk-powder	Cow
	Jørgensen	2005	Western Europe	Raw milk	Cow
	Pereira	1996	South America	Cheese	Cow
	Simeão do Carmo	2002	South America	Raw milk, unpast. cheese	Cow
	Taylor	1954	New Zealand	Raw milk	Cow
Streptococcus	Barnham	1983	UK	Raw milk	Cow
	Barnham	1987	UK	Raw milk	Cow
	Benson	1923	North America	Raw milk	Cow
	Campbell	1993	UK	Raw milk	Cow
	Edwards	1988	UK	Raw milk	Cow
	Francis	1993	Australia	Raw milk	Cow
	Henningsen	1938	Western Europe	Raw milk	Cow
	Kuusi	2006	Western Europe	Raw milk	Goat
	Lee	2001	UK	Raw milk	Cow
	Torre	1990	Western Europe	Raw milk	Cow
Toxoplasma	Riemann	1975	North America	Raw milk	Goat
	Sacks	1982	North America	Raw milk	Goat
	Skinner	1990	UK	Raw milk	Goat
Multiple pathogens	Gillespie	2003	UK	Raw milk	Cow
Multiple pathogens	Headrick	1998	North America	Raw milk	Cow
Unknown	Centers for Disease Control and Prevention	1984	North America	Raw milk	Cow

Appendix IV: Bibliography of Type 2 studies

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Appendix VI: Workshop report

Workshop on systematic review of the human disease evidence associated with the consumption of raw milk and raw milk cheeses

Thursday, 3rd July 2008, IVABS meeting room, Massey University, Palmerston North

Workshop report prepared by Patricia Jaros and Naomi Cogger

Report submitted on 10 July 2008

Aim

Detailed scoping of the systematic review

Participants

NZFSA	Public Health Unit	Fonterra
Donald Campbell	Jill McKenzie	Lindsay Pearce
Dianne Schumacher		
Sally Hasell		

Massey/IVABS	EpiCentre
Steve Flint	Naomi Cogger
Patricia Jaros	

Introduction

NZFSA - Overview of project

Previous literature reviews have described the literature relating the risk to consumers from the consumption of raw milk and raw milk cheeses. However, none of these have evaluated the quality of the information that is there in a 'systematic review' of the subject matter. Therefore, there is a need to conduct such a review. The current project will conduct a systematic literature review of the risk to human consumers. The review will be used as a reference (or basis) documentation for development of 'Standards' and potential policies permitting commercial sale and/or importation of raw milk and raw milk cheeses and for further risk analyses.

Massey University - Overview of approach

Project personnel proposed conducting a literature search and critical evaluation of the available data (= a systematic review evaluating internal and external validity). In addition, the project will determine if the data are of sufficient quality to warrant a meta-analysis. However, a meta-analysis will NOT be conducted as part of this contract.

Products to be considered in the review

The literature searching should focus on publications with food safety aspects and distinguish between raw milk, raw milk products (e.g. Mexican cheeses, Roquefort), and untreated by-products of raw milk (e.g. cream, raw milk butter, fermented products, yoghurt, butter milk, whey – excluding ice cream) as possible causes of human diseases; study quality and data are to be assessed critically. It is assumed the majority of articles/studies are presented as outbreak investigations or case descriptions – rarely as observational studies (e.g. cohort, cross-sectional, or case-control studies).

Pathogens – Human diseases to be considered in the review

Literature reporting human disease incidences associated with the consumption of raw milk and raw milk cheeses of bovine, goat, sheep, and buffalo origin are the main focus of this review. Major pathogens and related diseases to be considered are:

- *Campylobacter* spp.
- *Salmonella* serovars
- *E.coli* spp.
- *Listeria monocytogenes*
- Tuberculosis (*M.bovis*)
- *Bacillus cereus*
- *Brucella* spp.
- *Streptococcus* spp.
- *Yersinia* spp.
- *Staphylococcus aureus*
- *Shigella*
- *Toxoplasma*
- Q fever (*Coxiella burnetti*)

Keywords for database search

Following keywords are suggested to be included in electronic database searches: diseas*[13], zoonos*, epidemi*, public health, food borne illness, food poisoning, infect*, outbreak/case-control/cohort, death, fatality, mortality, morbidity, abortion (clinical description), miscarriage (clinical description), pathogen's name, (drinking) milk, dairy milk, bovine milk, cheese*, raw, unprocessed, untreated, unpasteur*, species (goat, sheep, dairy, buffalo).

[13] diseas* will find records containing any of the words beginning with diseas (e.g. disease, diseases). The asterisk can be used with any search term.

Sources of information

Electronic article databases Web of Knowledge (cross-searching of Web of Science, CAB Abstracts, Current Contents, AGRICOLA, and PubMed), ScienceDirect, PubMed (via Medline) will be searched for publications relating to the review. Project personnel will also search Google Scholar, websites of food safety authorities of the UK, USA, Canada, Ireland, Australia, the European Union; and websites of public health and food agencies of Denmark and the Netherlands for related reports. Articles will only be included if they have an English language abstract or summary. Should the information in the summary suggest the paper may be valuable, project personnel may request a copy of the paper and have seek to have it translated. Within the EpiCentre we could translate papers written in French, German, Spanish, Thai, Chinese, Russian, and Czech. The group also noted that where accessible, University libraries should be searched for Master and PhD theses relating to the topic.

Newspaper articles or stories published on the web will NOT be considered in the systematic review.

The group also agreed to send any information that may be relevant to Patricia Jaros.

Ranking criteria of literature

Retrieved literature will be ranked according to its relevance. The group determined that the following should be included in the criteria:

- Countries equivalence to NZ
  For example studies/data from countries non-equivalent to New Zealand such as developing countries with poor health status, or ancient data should be ranked as 'low'.
- Year of incidence
- Type of study (outbreak = descriptive study, case report)

Draft/Final Report

Early September 2008, the draft report written in technical language is sent to Donald Campbell first, and then forwarded to Sally Hasell and Dianne Schumacher ('Standard' Group of NZFSA) for final adjustments. The final report of this systematic review is expected end of September 2008. The report (or paragraphs of it) will then be put on the NZFSA website.

The ‘Standard’ Group of NZFSA will present the outcome of the project in a meeting end of September/early October 2008 inviting all participants of this workshop.

Action items

NZFSA person (Dianne Schumacher) to send documentation about categories of dairy products (categories 1 to 3) to Patricia Jaros.

All other people present to send any information that could be relevant to Patricia Jaros.